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THE PHARMACOLOGY OF JUNCTIONAL TRANSMISSION.

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THE major viewpoint of all pharmacological discussions should be not what are the actions of the drugs under discussion, but why they act in this manner. We must not rest content to know that acetyl choline has such-and-such an action and that atropine does or does not antagonize it, but must ask how acetyl choline so acts and what is the mechanism of the antagonistic action. This necessitates a wider approach to the subject, which perhaps falls more appropriately under the heading of the mode of action of drugs on cells. This is the spirit in which the present subject is approached.

General Pharmacological Considerations.

Let us first consider the general pharmacology of these substances which fall within the purview of this discussion.

In this paper it is intended to show that the common conceptions of the actions of the humoral transmitters may need revision and that transmission at the three main junctions is not by the same mechanism in each case. At the neuro-muscular junction the mechanism, according to the latest view, is humoral (acetyl choline); in the sympathetic ganglia the results at present are indecisive, whilst at synapses within the cord transmission appears to be wholly electrical. This is the general plan followed, but throughout the article other relevant information is given in brief and the reader should consult the original literature for further details.

Acetyl Choline.

In the main there are three sites in the body at which acetyl choline may act: (i) postganglionic parasympathetic nerve endings, (ii) all ganglia in the autonomic system, (iii) nerve endings for striated muscle. Pharmacologically the second and third sites may be combined because atropine is without action at these sites and curare is the antagonist, while at the first site the reverse holds. Furthermore, modern work emphasizes the homology of the ganglion and the end-plate region.[7] In all three cases the action is synergized by any substance which will nullify the action of choline esterase, such as eserine, "Prostigmin" or the new powerful antiesterase diisopropyl fluorophosphate (DFP).[8] As we shall see, both statements are over-generalized and it is gradually becoming clearer that all inferences from evidence of a pharmacological nature must be made with caution.

Adrenaline.

Adrenaline is the other humoral transmitter. It is formed at the ends of post-ganglionic sympathetic nerves, but, as will be shown, the action is not as simple as this. The action of adrenaline is twofold. It may cause either contraction or relaxation of the smooth muscle cells of the blood vessels of the body. The question is: how is this dual action brought about? Are the cells which respond to adrenaline in such a contrary manner the same or are there two different sites of action? On any theory of drug action it is difficult to see how one drug can induce in one cell changes in opposite directions at different times. The following experiments which we have carried out illustrate this complexity. It has long been known, but not generally recognized, that in some animals, normal except for anæsthetization, adrenaline will produce a fall in blood pressure.[1] However, the frequency with which the phenomenon is obtained is greatest in association with ether anæsthesia, which raises the blood pressure, and rare with chloroform anæsthesia or after decapitation, each of which lowers the blood pressure. From this it may be concluded that the response of an animal to adrenaline is not so much a function of the drug as a result of the environment of the cell at that moment, that is, it depends on whether the pressure is high or low.

To explain the anomalous action of adrenaline in these animals (cats) is difficult. It is not that the individual cats behave atypically, for a cat which at the commencement of an experiment may respond with a fall to all doses of adrenaline may later on respond with a rise, especially if the blood pressure should fall slightly; more rarely the opposite may happen. Two explanations are possible. The first is that all smooth muscle cells of vessels are identical and may, according to the pressure on them, be contracted or relaxed by the same drug. This seems incredible and is certainly impossible on the cell receptor theory of Clark. The alternative is that there are two types of cells present, one contracting in response to adrenaline and the other relaxing.

As with acetyl choline there are antagonists and synergists for adrenaline. Cocaine synergizes with adrenaline, but in this case we have not such a ready explanation as we have in the case of eserine and acetyl choline. Antagonism to adrenaline is exhibited by ergotoxine and yohimbine. Not only is there antagonism but apparent reversal of action. This "vasomotor reversal", as it is called, occurs in its simplest form after the administration of yohimbine; that due to ergotoxine occurs only after this drug has caused a rise in blood pressure, a condition which we have seen can by itself induce adrenaline to reverse its action. This objection does not apply in the case of yohimbine.

Nicotine.

Nicotine is our next instrument for functional dissection. The usual statement is that nicotine first stimulates then paralyses ganglia; but is this the whole action? We have recently reinvestigated the action of nicotine and have found that the results which we have obtained by ringing certain pharmacological changes cannot be explained along the usual classical lines.[2] When nicotine is injected intravenously there is a rise in blood pressure; this is thought to be due to stimulation of sympathetic ganglia with the resultant liberation of adrenaline at the endings of the post-ganglionic fibres. If this were so, then after the exhibition of yohimbine nicotine should produce a fall in blood pressure. This is not the case; the rise may be lessened, but only under exceptional circumstances is it abolished. Two explanations are possible. The first is that nicotine itself constricts certain vessels and that this action is not affected by yohimbine; the result of this constriction cancels out the fall which would have been caused by the depressor fraction of the sympathetic system. The second explanation is that nicotine does not stimulate those cells in the ganglia the post-ganglionic fibres of which innervate smooth muscle cells which bring about dilatation of vessels. This radical suggestion, which is put forward with some hesitation, will be expounded more fully later in the light of further supporting evidence.[2]

Curare.

From the modern viewpoint the academic curiosity curare is the most important pharmacodynamic substance for the investigation of junctional transmission. Curare, besides paralysing voluntary nerve endings, also paralyses transmission through ganglia. This is a general property of nearly all quaternary ammonium compounds, and it is only recently that any attention has been paid to the importance of the chemical properties of alkaloids in which the nitrogen is in the tertiary or quaternary form. There are many differences to be considered, such as solubility in water and lipoids, degree of ionization *et cetera*. There are also many anomalies to be explained away. Tetramethylammonium iodide is curariform, the ethyl compound is not; "Eumydrin", the quaternary derivative of atropine, still retains many of the atropine characteristics. More will be heard of these quaternary compounds in the future as substitutes for curare as an adjuvant to anæsthesia.

Inorganic Ions.

When, however, we turn to consider the action of the inorganic ions at the synaptic and other junctions, all the paradoxes of the alkaloids fade by comparison into a charming simplicity. The elucidation of the role of potassium and calcium in humoral transmission is fraught with difficulties because of the contradictory nature of the results. In general it may be said that potassium mimics acetyl choline and calcium adrenaline. Recently we have had an inkling of the part played by calcium in the action of certain drugs.[3] Quinine, yohimbine and strychnine decrease the amount of physiological calcium present in solution and, in reality, some of their action can be explained as calcium lack. In addition, for repeated stimulation of striated muscle quinine has a slight curare-like action and this is the basis for its use in the treatment of *myotonia congenita*[5] and as a diagnostic test for *myasthenia gravis*.

With regard to the action of calcium, quinine, yohimbine *et cetera*, it has been shown[4] that less reliance is to be placed on the specific chemical structure of a drug as a guide to its pharmacological properties than has been the custom in the past, and that many drugs seem to fall into groups with a pattern of action that is unrelated to their structure.

Junctional Transmission.

Let us now turn from a consideration of the pharmacology of the humoral agents to the specific problem of the transmission of the impulse across these gaps.

The Neuro-Muscular Junction.

We shall consider first the neuro-muscular junction, because here the entire plan has worked out in detail in one period of time and this plan will serve when we come to consider transmission elsewhere. If a muscle is perfused, stimulation of the motor nerve leads to the appearance of acetyl choline in the perfusate. Close intraarterial injection of acetyl choline produces a result mechanically and electrically identical with that obtained from nerve on stimulation. Under suitable conditions eserine changes the response of muscle to a single nerve volley from a brief twitch to a brief waning tetanus, which produces a tension twice that of a normal twitch. This, of course, supports the belief that acetyl choline is involved.

The study of the action of curare has been of the greatest importance. It does not prevent the liberation of acetyl choline, only its action. By partial curarization it has been possible to eliminate the spike (the electrical manifestation of the propagated contraction, which interferes with the investigation of the end-plate transmission) and to demonstrate the existence of an earlier electrical activity in the end-plate which is referred to as the end-plate potential (epp).[6] As we shall see, the end-plate is directly excitable by acetyl choline and potassium, and when it is so excited an end-plate potential is produced.[11] Having shown the existence of the end-plate potential and its importance, it is now necessary to return and consider the action of eserine on transmission and the bearing which it may have on the acetyl choline mechanism. In the non-curarized preparation, after the exhibition of eserine, single nerve volleys cause an increase and lengthening of the local negative potential which is produced at the end-plate and which persists beyond the muscle spike. The spike itself is not changed. The end-plate negativity of the eserinized muscle shows two waves of depolarization: (i) a lengthened end-plate potential and (ii) a "slow wave" with a delayed rise and a very slow decay, which is more affected by eserine. The onset of the slow wave merges more or less with the decaying phase of the end-plate potential. The declining phase of the end-plate potential is a passive electrotonic one; the transmitter action is much shorter than the end-plate potential which it produces, and the principal action of the eserine is to lengthen the action of the neuro-muscular transmitter, thus leading to prolonged junction negativity with catelectrotonic effects, such as repetitive muscle spikes, lengthening of the refractory period and, during very intense depolarization, a complete block of impulse propagation.[9] The local effects of depolarization of the muscle at and around the end-plate are analogous to those of cathodal currents applied artificially. This dual nature of the potential at the end-plate, which is seen particularly with repetitive

nerve volleys in an eserinized muscle, was for a time puzzling. If the transmission was due only to acetyl choline, then eserine, "Prostigmin" and a background of acetyl choline at the end-plate should affect both parts of this potential equally. In the earlier work this was not so, but recently Eccles (personal communication) has said that he is convinced that transmission at the end-plate is entirely due to acetyl choline.[10] That is to say, the evidence from the action of eserine and a study of the effect of a "background" of acetyl choline is such as to enable the hypothesis to be made that acetyl choline is formed at the endings of the motor nerves; this spreads by diffusion and sets up an end-plate potential; this in turn serves as a source of current and the muscle fibre is stimulated by catelectrotonus. The decay process of the transmitter (acetyl choline) is probably purely one of diffusion.

Further support for the acetyl choline hypothesis is provided by the extremely ingenious experiment of Kuffler[11] in which he applied drugs to the "nervous" and nerve-free region of the sartorious muscle and to the end-plate and other regions of a single nerve muscle fibre preparation and recorded the potential changes at the place of application. He was able to show that acetyl choline, nicotine *et cetera* set up impulses by depolarizing the muscle membrane at the end-plate region. None of the drugs appreciably depolarized the end-plate-free parts of the muscle or set up impulses there. Potassium initiates impulses at the end-plate region and along the muscle fibre because it is able to depolarize the membrane of the cell. Curarine opposes the depolarization and excitation caused by drugs but not that caused by potassium.[12] The failure of acetyl choline to set up impulses at the end-plate-free parts of muscle seems to be adequately explained by the absence or smallness of its depolarizing action at these regions.[13]

Kuffler[12] has also studied the effect of excess ionized calcium which gradually blocks transmission, probably by lowering the electrical excitability of the fibre adjacent to the end-plate. Reduction of the amount of calcium to one-quarter causes increased excitability and increased sensitivity to acetyl choline which results in repetitive response to a single nerve stimulus. A block then develops, although the nerve endings still conduct impulses, and the action potential from direct stimulation is not altered, but the end-plate potential is diminished. It is suggested that the block is due either to diminished production of transmitter or to decreased excitability of the end-plates. The spontaneous activity resulting from immersion in citrate solution or calcium-free solution originates primarily in the end-plates. If part of the sartorius muscle is lowered into calcium-free saline solution it becomes negative relative to the rest of the muscle. Once again the importance of the end-plate region is emphasized. Potassium, which, of course, causes contraction, has been shown to be essential for the passage of the impulse. The action of potassium ions on the end-plate is first to facilitate transmission and then to depress it. It is suggested that both these effects of potassium may involve alteration in the size of the end-plate potential and in the excitability of the muscle fibres.[14] Eccles has also suggested that potassium stimulates the nerve endings to exhaust their supply of acetyl choline and that this accounts for the depression.

The antagonism between eserine and curare is of extreme interest from the point of view of the mode of action of drugs. The above actions of eserine are all antagonized by curare, which appears to have three actions: (i) it obliterates the slow wave component, (ii) it reduces the end-plate potential, (iii) it abolishes the after-discharge from the nerve terminals. In other words, it is a depressant of the excitatory responses evoked in the end-plate by acetyl choline and related substances. In the curarized muscle the end-plate potentials sum, and if a certain level is reached and a spike may result, eserine abolishes this spike. As is well shown by in-vitro experiments, the curare does not antagonize the esterase-eserine combination; it does not quicken accommodation to acetyl choline. The most interesting point is that it is an antagonism between a tertiary and a quaternary compound, substances which are supposed (because of different solubility and ionization properties) to act at different parts of the cell.[10]

Scheinfinkel[15] has endeavoured to show a dissociation between acetyl choline and electrical stimulation. He finds that stretch reduces the effect of chemical stimulation but not that of electrical stimulation, while electrically fatigued muscle is still highly responsive to acetyl choline. Buchthal[16] brings the work into line with current biochemical theories for the supply of energy for contraction by showing that adenyltriphosphate in a concentration of 10^{-5} microgramme applied to even curarized isolated muscle fibres causes a tetanus-like contraction which is accompanied by an action potential. This compound also increases the sensitivity of the muscle to acetyl choline and to electrical stimulation.

Perhaps the most remarkable phenomenon is that in the cat, in which there are repetitive discharges (antidromic) originating from the nerve terminals of the eserinized muscle, the cause of which is unknown; they may also be invoked by intraarterial injection of acetyl choline in the normal preparation.[17] If the muscle is stimulated, antidromic impulses will be found in the nerve only if the animal is eserinized; this is referred to as retrograde transmission. This retrograde transmission suggests that repetitive muscle spikes, which arise from prolonged end-plate negativity, would be responsible for some of the nerve discharge. However, there is no doubt that some nerve discharges are independent and prior to muscle discharges.[9]

Another valuable weapon in the electrophysiologist's armoury is veratrine. The production of contracture by this compound interested early workers, and later its most striking action on the negative after-potential of nerves led to the establishment of the identity of this potential. Recently attention has been focused on its action on the muscle membrane and neuro-muscular transmission.[18] Veratrine increases the negative after-potential following a muscle spike. The negative after-potential is gradually built up and resembles the potential changes caused by depolarizing drugs or by catelectrotonic current pulses. If the potential attains a critical height muscle impulses are initiated. The resulting potential and spike are unaffected; nor are the transmitter action and sensitivity to acetyl choline and potassium affected. The essential action of veratrine on the muscle concerns processes which occur only after the impulse. Accordingly it is suggested that the negative after-potential is produced prior to and is independent of the contraction. Kuffler concludes by saying that at the present no indication of the nature of the link between muscle membrane and contractile elements has been found. It seems, however, that action currents flowing during depolarization do not play an essential role in the excitation of the contractile system. For instance, for a muscle which is entirely immersed in a contracture-producing solution, the whole membrane will be simultaneously depolarized. It is clear that in such cases no current flow from the "normal" to the depolarized region can occur. Contractures covering a large area, or those produced over a few millimetres, will be inhibited at the anode of a constant current pulse. It seems, then, that a drug like potassium or acetyl choline produces its contracture by removing at least part of the membrane potential. Any process restoring the membrane to its polarized state causes a relaxation of the contracture. On withdrawal of the anodal current the depolarizing effect of the drug, if still there, will be reasserted and will again set up a contracture. Since it appears that there is no essential difference in the setting up of twitch-contractions and contractures, it would appear also that the currents of a propagating muscle impulse have no direct excitatory effect on the contractile elements.[13]

The Sympathetic Ganglia.

We now turn to the sympathetic ganglia,[19][20] in which it was early shown that acetyl choline appeared in the perfusate when the preganglionic fibres of a perfused ganglion were stimulated, and that the injection of acetyl choline into this preparation fired off impulses along the post-

ganglionic fibres. The presence of eserine enhanced both effects. During the perfusion of the ganglion with acetyl choline[24] submaximal volleys of pre-ganglionic impulses excite many cells that do not respond in the absence of acetyl choline. Against this is the assertion of Lorente de No[23] that acetyl choline does not appear in the perfusate until the ganglion is damaged by asphyxia or fatigue. However, one school would not accept acetyl choline as the transmitter. The reasons advanced were that the short synaptic delay and brief duration of the response process ruled out a chemical transmitter. Because a persisting quantity of acetyl choline causes sustained activity the neuro-humoral hypothesis must explain how a nerve volley initiates a single response at a synapse. The usual assumption is that it is inactivated by the choline esterase. Bruche and later Nachmansohn[21] have calculated that such a rapid removal of the acetyl choline could be brought about if the esterase were supposed to be concentrated in certain regions. How justifiable this and other assumptions are is debatable.

The early conflicting results of Brown and Eccles concerning the action of eserine have now been "ironed out". In general, eserine increases the synaptic potential (see later), but the effect is seen only with repetitive stimulation.[22] The after-potentials are likewise prolonged by eserine only after repetitive stimulation.

When we turn to the question of the inorganic ions the position is less clear. As is well known, potassium stimulates the ganglion and perfusion with potassium chloride increases the discharge initiated by a pre-ganglionic volley; it also liberates acetyl choline from innervated ganglia and in large doses paralyses them. Excess calcium blocks transmission, while a reduction in the amount of ionized calcium causes a spontaneous discharge and a repetitive after-discharge.

The main question is whether the action of potassium is prior to that of acetyl choline. If the ganglion is perfused with curarine, acetyl choline is liberated but is unable to act, while potassium can still initiate a discharge. The action of potassium is abolished by nicotine, but the salt can still cause an antidromic discharge along the pre-ganglionic fibres; thus the action of nicotine is located at the post-ganglionic cell.[25] It has been suggested that potassium is the transmitter and that it activates the pre-ganglionic elements; the release of acetyl choline could thus be due to non-specific activation of the pre-ganglionic nerve endings.

However, there are many experiments to show a dissimilarity between the action of acetyl choline and potassium, of which we may mention a few.[26] The raised blood pressure due to the nicotine-like action of acetyl choline is reversed by sparteine, but that due to potassium is reinforced. A denervated frog muscle is hypersensitive to acetyl choline but hyposensitive to potassium. Cobra venom, which blocks transmission of motor impulses, abolishes the response to acetyl choline but not to potassium. In the earthworm the synthesis of acetyl choline ceases in the cold; if potassium is added to the cold preparation it is without action; if the worm is warmed the potassium acts and its action is potentiated by eserine; this is taken to mean that potassium first liberates acetyl choline.[27]

The presence of calcium ions in the perfusing fluid is essential both for the transmission of the impulse and for the formation of acetyl choline when the preganglionic nerve endings are stimulated. When the calcium ions are decreased the ganglion cells exhibit long, continuous, spontaneous activity in the form of a repetitive discharge.

Recently, Eccles[28] has brought transmission in the synapse into line with neuro-muscular transmission. He placed an electrode at the pole of the stellate ganglion and an electrode at the cut ends of the cardiac nerves and administered curarine. A single pre-ganglionic volley causes the development of a potential difference which is referred to as the "synaptic potential" and is likened to the end-plate potential. On successive stimulation summation occurs and the second synaptic potential is enhanced. As the frequency of stimulation is increased progressive fusion of synaptic potentials occurs. As the curarization decreases the summation of the two synaptic potentials results in the initiation of a propagated spike. The synaptic potential is not significantly altered by eserine. On repetitive stimulation the negativity of the ganglion is prolonged by eserine. Eserine has no action on ganglion potentials antidromically evoked. Analysis of synaptic changes indicates a "peak" and "tail" action; neither is affected by eserine. The properties of the "tail" action suggest that it may be due to a choline esterase-resistant substance liberated by pre-ganglionic stimulation. It is proposed that the "tail" action is due to acetyl choline which is removed by an eserine-resistant mechanism such as resynthesis to its precursor and partly by diffusion to the "barrier" of esterase. The action of eserine is to inactivate this barrier and the acetyl choline is free to spread along the surface membrane and exert an action lasting for some seconds. After-discharge, in either the normal or eserinized ganglion, is set up by repetitive pre-ganglionic stimulation when the acetyl choline accumulates above a threshold concentration.

In summary, the following hypothesis of synaptic transmission seems best in accordance with the experimental evidence, though many other possible explanations could be devised. A pre-ganglionic impulse exerts a brief depolarizing action on the ganglion cell by the direct effect of its action current (the peak action). Superimposed on this depolarizing action at the beginning and long outlasting it is the tail action due to the liberated acetyl choline (and possibly to other substances such as potassium ions). The acetyl choline is removed from the locus of action by some eserine-resistant mechanism, such as resynthesis to its precursor, but also partly by diffusion to the surrounding barrier of choline esterase, where it is rapidly hydrolysed. Eserine inactivates this barrier and acetyl choline is then free to spread along the surface membrane and exert its action for some seconds. After-discharge, in either the normal or eserinized ganglion, is set up by repetitive pre-ganglionic stimulation when the acetyl choline (or other exciting substance of the tail action) accumulates over a threshold concentration.

Burn[30] has reinvestigated the action of adrenaline on junction transmission. The Orbeli phenomenon is due to the action of adrenaline on the end-plate rather than on the muscle itself. In the spinal cord reflexes are facilitated by the presence of adrenaline, which appears to have three actions: (i) it potentiates the action of acetyl choline, (ii) it intensifies the effect of "Prostigmin", (iii) it influences transmission along the nerve. Finally, Burn claims to have demonstrated the liberation of adrenaline in the synapse during the passage of an impulse and this is supposed to facilitate transmission. This is contrary to the findings of Marrazzi,[31] who claims that the primary action of adrenaline is to produce depression in the ganglion.

The Spinal Cord.

It was natural that the thoughts of physiologists should now turn to transmission within the central nervous system. As one would expect, the results are confusing, even though Feldberg[32] has tried to reduce them to a semblance of order. Acetyl choline and the esterase both occur in this issue, which also possesses the ability to synthesize acetyl choline. The effects of the injection of acetyl choline and eserine are various; usually they are stimulatory and atropine generally abolishes this effect.

Eccles[34] has shown that to a certain extent events in the motor neurones of the spinal cord follow those in the sympathetic ganglia and the neuro-muscular junction. Experimentally a volley is sent in by the dorsal root and the leads are taken from the corresponding ventral root on the same side. To eliminate the electrical effects of the spinal reflexes "Nembutal" was used. This is to be compared with the use of curarine to block transmission at the neuro-muscular junction and show up the end-plate potential. When curarine was used for this purpose in the spinal cord it brought about a convulsive (electrical) discharge resembling the action of strychnine. A single stimulation of the dorsal root led to the development of a brief negative potential charge in the ventral root. It had a much slower time course than the spike which was

produced in the absence of "Nembutal". This potential is referred to as the synaptic potential and is homologous with the synaptic potential of the sympathetic ganglion and the end-plate potential. It is due to electrotonically leading-out potentials generated within the spinal cord and led out by the ventral roots. The central locus of the catelectrotonus occurs in the soma of the motor neurones belonging to the fibres of the ventral root. The synaptic potential exhibits the characteristic shape of catelectrotonic junction potentials—an S-shaped rise to a rounded summit and a decay which is approximately exponential in its latter part. Summation is evident with two volleys. Without the exhibition of "Nembutal" the synaptic potential can be shown to begin before the discharge of the motor neurones. The synaptic potential has been analysed on the basis of Hill's local potential theory in order to obtain a time course for the transmitter action. The actual transmitter action curve is such a brief peak that it could be caused by the action currents of impulses impinging on the synapses. There is no appreciable tail in the transmitter action such as was observed in the synaptic potential of the stellate ganglion. Correspondingly repetitive stimulation has given no evidence of the accumulation of a synaptic transmitter such as was observed in the stellate ganglion and attributed to the summation of some chemical transmitter.

Eserine was without action on the synaptic potentials even after repetitive stimulation. This contrasts with the sympathetic ganglia, in which prolonged negative potentials were built up by the repetitive stimulation of the eserinized ganglion but not of the normal ganglion. Similarly, soaking the cord in a solution containing acetyl choline 10^{-3} gramme had only a mild depressant action on the synaptic potential.

The use of "Nembutal" as a pharmacological tool to suppress motor activity is most interesting.[1] We have done a considerable amount of work with the barbiturates and, following up the work of Gruber, have shown that these compounds act at all junctional areas in the body rather than on the nerve fibres; although if present in sufficient amounts (2%) they will block reversibly the transmission of the nerve impulse. There is also a mutual antagonism between the barbiturates and eserine. "Amytal" prevents the liberation of acetyl choline on stimulation of the vagus nerve to the intestine, as Trethewie[28] has shown. It is possible that the non-activity of eserine does not rule out the conception that acetyl choline does play a part. A further sidelight on this work is a suggestion of Brooks[33] that "Nembutal" stabilizes the membrane against breakdown by electrotonic currents; this, if true, will have great bearing on the mode of action of barbiturates in anæsthesia.

Thus it may be concluded that the experimental evidence strongly indicates that acetyl choline plays no significant role in synaptic transmission in the monosynaptic pathway through the spinal cord. The effects it produces would appear to be of pharmacological interest only. With the sympathetic synapses it was shown that acetyl choline exerts a long transmitter action giving after-discharge after repetitive stimulation; the initial brief transmitter action gave every indication that it was due to the action currents of the pre-ganglionic fibres. With synapses of the spinal cord only this brief synaptic potential can be detected, and it gives every indication that it is produced by the direct electrical excitatory effect at the synapses of action currents in the dorsal root fibres. Finally, the simplest time course for reflex facilitation in the frog is in excellent agreement with the time course of the synaptic potential. There is no doubt that all phenomena attributable to the central excitatory state (c.e.s.) may now be explained in terms of the synaptic potential.

The Formation of Acetyl Choline.

If acetyl choline is to play such an important role at certain junctional regions it is natural that its formation at these sites should be of interest. Quastel[35] and others have demonstrated that acetyl choline is formed in brain slices, that is to say, in intact cells, but under aerobic conditions and only if glucose or pyruvate is present. The final mechanism of this synthesis has not been elucidated. Nachmansohn[36] has been able to isolate from brain a cell-free acetone extract which is capable of synthesizing acetyl choline in the presence of eserine; this excludes the possibility that it is due to the reverse action of choline esterase. The reaction mixture consists of the extract (the enzyme has been called choline acetylase), choline, acetate, eserine and, finally, adenosine triphosphate to provide the energy. The synthesis is also enhanced by the presence of potassium ions. Substances which react specifically with SH groups poison the enzyme, so it is thought to belong to the large group of enzymes in which the protein contains SH groups. Accordingly cysteine and cyanide increase the activity of the enzyme. More recently the presence of a coenzyme has been recognized, since after dialysis the preparation is inactive, although the activity is restored to a certain extent by glutamic acid. It may also be completely restored if an extract of such tissue as brain, liver, heart or muscle is added.

Feldberg[37] has worked along similar lines to Nachmansohn and has found the following to be necessary for synthesis: (i) choline, (ii) adenyl triphosphate, (iii) citrate, and (iv) an activator which may be identical with the above coenzyme. Very little synthesis takes place if only one of the last three is present; if, however, any two are present, then synthesis is almost at a maximum. In the system which includes citrate, magnesium and manganese ions have a great accelerating effect.

Can we give any explanation of the action of potassium and calcium in terms of their relationship to acetyl choline synthesis? Potassium accelerates and calcium diminishes formation of acetyl choline in respiring brain tissue, and calcium, in the presence of adenyl triphosphate, prevents the building up of a store of acetyl choline in the tissue particles of dried brain suspension. Calcium ions inhibit the breakdown of adenyl triphosphate, but potassium ions do not affect the dephosphorylation. Therefore the antagonistic action of these ions is not associated with the adenyl triphosphate and there must be yet another factor connected with the synthesis of acetyl choline in which the two ions are involved. The above work refers to the synthesis of acetyl choline from choline; it does not refer to its liberation at the moment of action. There have been several suggestions that it is split and resynthesized into a precursor. In nerve it is supposed to result from the mobilization of potassium ions. If the cervical sympathetic trunks are cut, the distal part and the ganglion lose their power to synthesize acetyl choline in about two days; at the same time the acetyl choline content drops and conduction is impaired. All this leaves the question still in doubt.

Conclusion.

In conclusion, it is apparent that the older ideas of the action of adrenaline and nicotine may undergo some revision from the rather rigid conceptions existing at present. The present view is that transmission at the neuro-muscular junction is due to the liberation and diffusion of acetyl choline at the end-plate region, but that surprisingly enough choline esterase plays small part in its initial removal from the site of action. The position in the sympathetic ganglion is doubtful, although the acetyl choline mechanism is most likely. In the central nervous system acetyl choline seems to have no normal function in transmission, this being purely electrical, and any pharmacological action which it may have when applied to the synapse is entirely accidental. This last extreme view depends upon our conception of the term electrical, and if, as is possible, the electrical manifestations are but part of some chemical process of an ionic nature, then we may expect in the future a further reconcilation of the chemical and electrical viewpoints.

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ELECTROENCEPHALOGRAPHY: THE LOCALIZATION OF CEREBRAL LESIONS.

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IN most countries electroencephalography is an accepted diagnostic aid in neurological disorders. In Australia it is not a familiar method, because until recently Sydney has been the only active electroencephalographic centre. The purpose of this communication is to illustrate the method simply and to indicate the scope of electroencephalography as an aid to the diagnosis of focal brain disease. Before we embark on this a general account of the principles involved and of the findings in normal subjects may not be out of place. For a broader survey reference should be made to the recent short review of Williams,(1) which has a full bibliography, and to the standard texts of Jasper(2) and of Gibbs and Gibbs.(3) A brief account of the electroencephalogram has also been given by Phillips.(4)

Method.

The electroencephalogram refers to the record of the electrical potential variation derived from the brain, which can be recorded from electrodes attached to the scalp surface. The electrodes, which may vary in type, number and placement, are led to the inputs of thermionic valve amplifiers, and the voltage differences existing between the electrodes are magnified about 10,000,000 times, so that sufficient power is given to drive an electromagnetic or other ink-writing oscillograph. In localization work it is necessary to refer back to the record as it is being taken, so that the proper combinations of placements may be selected. For this reason the ink-writer is the only type suitable for clinical electroencephalography.

The electroencephalograph itself comprises a number of independent amplifiers (or channels) and a corresponding number of oscillographs. The minimum requirement for ordinary use is three channels; four are preferable and six are now regarded as the standard number. All records shown in this paper were obtained with a Clifton ink-writing electroencephalograph, the paper speed being three centimetres per second. All traces illustrated read from left to right. During the recording the patient sat or lay in a dimly illuminated, electrically shielded room. Quietness and relaxation are essential for satisfactory recording.

The Normal Electroencephalogram.

With these standard conditions the normal electroencephalogram may be obtained with the following characteristics.

The β rhythm has been defined as a rhythm of about 25 cycles per second associated with the precentral areas. It is of much lower voltage than the α rhythm, and as it is not important for this paper it will not be discussed further.

The α rhythm is a rhythmic sinusoidal electrical activity of a stable frequency lying between eight and twelve cycles per second. It can usually be recorded from all head regions when the eyes are closed. It is maximal in the parieto-occipital lobe, and its voltage may vary from less than five to more than 100 microvolts (millionths of a volt). A convenient and simple grouping of α rhythms is that of Walter,(5) in which the division is into low, medium and high voltage types.[2] These three types are illustrated in Figure I.

The α rhythm, for purposes of description, may be said to be due to the resting activity of cells in areas 18 and 19 of the parieto-occipital cortex. It is synchronous and symmetrical in each hemisphere and may be controlled

[1] Assisted by a grant from the National Health and Medical Research Council.

[2] The grouping given here is a modification of that of water.

by a subcortical pace-maker (Adrian and Matthews[6]). Normally it is readily abolished by attention stimuli, especially by a request to the patient to open his eyes. He then sees objects and shapes, and the visual association areas are no longer in a resting state. The α rhythm may also be blocked by intellectual activity; for example, mental arithmetic (which in most people is probably associated with active visual imagery) is especially potent in abolishing the α rhythm. Pain has a similar but less pronounced effect. Noise, particularly in the case of patients who have been blind for many years, will interfere with α rhythm activity.

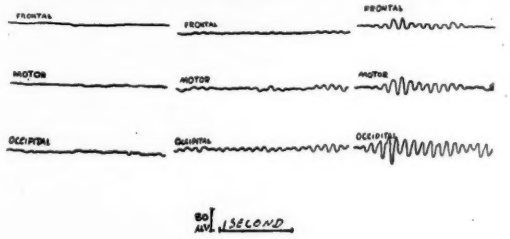

FIGURE I.

Three normal electroencephalograms showing the three main types of α rhythm—low, medium and high voltage. The horizontal line in this and subsequent figures indicates a period of one second. The vertical line denotes the voltage in microvolts (millionths of a volt).

In normal persons the α rhythm is about equal in voltage in each hemisphere, and there is strong evidence that it is propagated forwards from an "α focus" by the long association fibres, lesions of which are followed by loss of α rhythm at and anterior to the site of interference. Destruction of the α focus itself causes an absence of the α waves over the whole ipsilateral hemisphere (Williams and Reynell[7]). A pronounced difference in voltage between hemispheres is termed "amplitude asymmetry" and is always abnormal.

The presence of amplitude asymmetry may be used in the localization of cerebral lesions, as is illustrated in the first two cases.

CASE I.—The patient was a female, aged thirty-seven years. Five months ago she noticed that her vision was impaired on the right side. Examination of the visual fields revealed right homonymous hemianopsia with macular sparing. Air studies (encephalography) revealed atrophy of the left occipital region, the posterior horn of the left lateral ventricle being dilated and drawn to the left. A clinical diagnosis was made of a vascular lesion, probably thrombotic, on the left side. This was supported by the electroencephalogram, which showed no α rhythm from any part of the left cerebral hemisphere, but a medium voltage normal rhythm from the right (Figure II). The patient is alert, intelligent, and apparently in good general health.

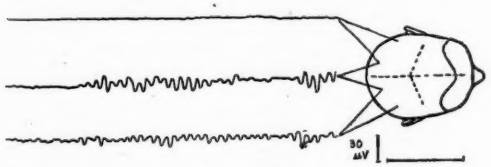

FIGURE II.

Case I. Amplitude asymmetry in lesions of the parieto-occipital region. In each case a stable α rhythm is present on the normal side, but on the affected side there is hardly any normal activity. See text for details.

CASE II.—The patient was a male, aged nineteen years. As a result of birth injury he developed wasting and deformity of the left arm, and since infancy he has had Jacksonian seizures affecting the whole of the left side. Examination revealed that the plantar reflex was extensor in type and that the tendon reflexes on the left side were exaggerated. The visual fields were also abnormal; right homonymous hemianopsia was present, and macular vision was not spared. Air studies (encephalography) showed that the right lateral ventricle was grossly dilated, and in the occipital regions it extended to the brain surface, closely approaching it in the temporal region. The electroencephalogram showed an almost total absence of α rhythm on the right side, while the left appeared normal (Figure III). In contrast with the previous case, this patient is a crippled, mentally retarded invalid.

Comment.

These two cases illustrate that the electroencephalogram has meaning only in relation to the clinical findings. Taken alone, the two records are almost identical (although different sides are affected); but the contrast in the clinical picture is striking. The common neurological feature is damage to the visual association areas and to the calcarine fissure. The interference with the former has in each case resulted in pronounced amplitude asymmetry, and this is all that the electroencephalogram shows.

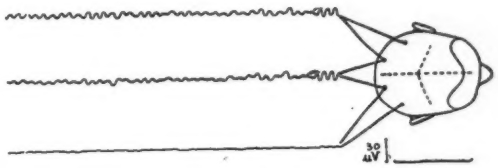

FIGURE III.

Case II. Amplitude asymmetry in lesions of the parieto-occipital region. In each case a stable α rhythm is present on the normal side, but on the affected side there is hardly any normal activity. See text for details.

Focal Abnormal Rhythm.

So far we have dealt with the absence of normal rhythms as an aid to localization. In the following cases the detection of focal abnormal rhythms is considered. Cerebral lesions—tumours for example—may give rise to abnormal wave forms—namely, δ waves, "saw-tooths" and "spikes". The term "δ" was introduced by Walter[8] to denote all waves slower than seven cycles per second; but with the separation of the "θ" band of frequencies (four to seven cycles per second) as an entity, the term "δ" is sometimes reserved for frequencies of three cycles per second and less.

These δ waves may be recorded from all head regions in post-epileptic stupor, in full anæsthesia, in oxygen deprivation, in raised intracranial pressure and in many conditions which interfere directly or indirectly with normal cerebral metabolism.

As a localized phenomenon δ waves are often associated with focal cerebral disease. Their origin, however, is not the tumour, which is itself electrically inactive, but the neighbouring cerebral cortex, whose normal function is interfered with by pressure or traction. They may be of high or low voltage, and range from less than 20 to more than 200 microvolts. Abscesses and rapidly growing tumours give rise to high voltage activity. Benign tumours, such as meningiomata, may produce minimal disturbance or even none at all. In addition to slow waves, random very fast waves or "spikes" are characteristic of focal cortical discharge. The two are often seen in association in the one record.

Technique of Localization.

Local electrical abnormalities in cases of cerebral tumour were discovered in 1935 by Foerster and Altenburger[9] at operation; but Walter[8] was the first to demonstrate that cerebral tumours could be localized by means of electrodes placed on the scalp without exposure of the brain surface. He applied the "phase reversal" technique which had been devised by Adrian and Matthews[5] in their earlier work on the source of the α rhythm. This method depends on the fact that focal electrical abnormality may be picked up by one of the electrodes in the vicinity of the lesion. The principles are shown in Figure IV and

illustrated in Figures V and VI from two cases of cerebral tumour.

Case III.—The patient was a male, aged fifty-two years, who had suffered from frontal headaches for three months, with loss of memory and of initiative. Clinical examination revealed bilateral papilloedema; the plantar reflex on the left side was extensor in type. The cerebro-spinal fluid pressure was 290 millimetres of water, and the globulin content of the fluid was increased. The electroencephalogram showed generalized δ wave activity from all areas; but from an electrode placed over the right frontal lobe consistent phase reversals of the δ waves were noted, which suggested that

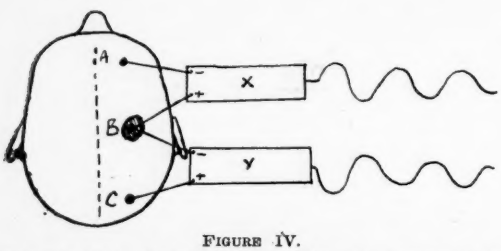

Figure IV.

The principles of phase reversal. In this diagram it is supposed that three electrodes, *A*, *B* and *C*, are affixed to the scalp and that one of them (*B*) is on an electrically active area. The electrodes are connected to the inputs of the two amplifiers *x* and *y*. The inputs are labelled "+" and "–". It will be seen that if the activity under *B* is recorded, then the adjacent traces must move in opposite directions, as *B* is linked to the "+" input of one amplifier and to the "–" input of the other. This is termed a phase reversal, and in this diagram slow waves are drawn. In actual practice many more placements are used. Actual phase reversal records are shown in Figures V, VI, VII and VIII.

this was the site of the lesion (Figure V). Air studies confirmed this, and at operation an extensive *spongioblastoma multiforme* was found in the precentral region, the site of maximal abnormal electrical activity being the cortex adjoining the anterior edge of the main neoplastic mass.

Case IV.—The patient was a male, aged forty-five years. He gave a history of failing concentration, loss of initiative, giddiness and frontal headache extending over a period of

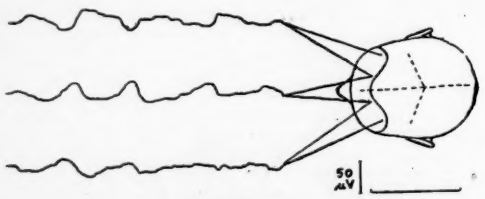

Figure V.

Case III. Phase reversal of δ waves in the upper two traces derived from the right frontal lobe; rapidly growing tumour in this region (see text).

four years. Clinical examination revealed left papilloedema, left anosmia and right ankle clonus. The cerebro-spinal fluid pressure was 240 millimetres of water; the globulin content of the fluid was not increased. A plain X-ray film of the skull revealed a calcified mass in the frontal pole, and a provisional diagnosis of meningioma arising from the *crista galli* was made. The electroencephalogram showed "spike" and δ phase reversals from an electrode placed six centimetres above the orbital margins in the line of the pupil. Recording from other placements suggested that the lesion was in the frontal lobe itself (Figure VI). At operation an oligodendroglioma in this situation was found and successfully removed.

Comment.—In these two cases the important electroencephalographic differences can be related to the clinical histories. In Case III the record was one of generalized δ wave disturbance in a patient with a short history of illness and rapid deterioration. Post-mortem examination of the brain revealed an invasive tumour, principally precentral, but with much wider involvement of cerebral structures than was at first supposed. In Case IV, however, the record showed abnormalities sharply restricted to one side, and the history was a long one, the tumour being benign and confined to the left frontal pole.

Localization of Epileptogenic Foci.

The next two cases illustrate the localization of epileptogenic foci by phase reversal. By an epileptogenic focus is meant an area of cerebral cortex which shows abnormal electrical activity and which gives rise to epileptic seizures which may be focal in character.

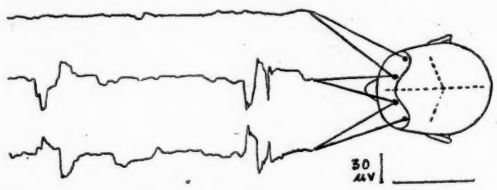

Figure VI.

Case IV. Phase reversals of "spikes" and slow waves in the lower two traces from the left frontal lobe in a case of slowly growing tumour (oligodendroglioma) of the left frontal lobe.

Case V.—The patient was a female, aged fifteen years. After a delayed and difficult birth the patient developed hydrocephalus and paresis of the right side. She is mentally retarded, and eight months ago began to suffer from Jacksonian seizures affecting the right side of the body. Air studies (encephalography) revealed a grossly dilated ventricular system, the left lateral ventricle being more affected than the right. The electroencephalogram showed an active epileptogenic focus with "spikes" and slow waves arising from a broad area over the left hemisphere and including the motor cortex.

Case VI.—A male patient, aged thirty-one years, had a history of severe birth trauma followed by convulsions. For fourteen years he has had *grand mal* seizures. Clinical examination revealed left homonymous hemianopsia and left hemianæsthesia. Air studies revealed enlargement of

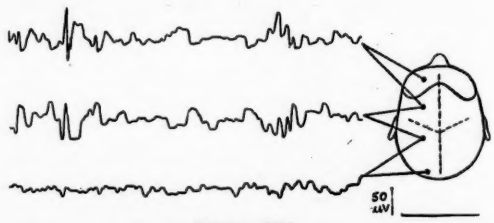

Figure VII.

Case V. Phase reversals of "spikes" and slow waves are seen in the upper two traces and indicate an epileptogenic focus in the left precentral region. Other portions of the record indicate that the discharging area extended back to the region of the central fissure. The electrical activity on the right side (not shown) is relatively normal. See text.

the right lateral ventricle and atrophy of the temporal and parieto-occipital cortex. At operation severe cerebral agenesis was present, with almost no cortical tissue in the parieto-temporal region, which was unresponsive to electrical stimulation. The electroencephalogram showed an actively discharging focus in the right occipital pole, and this probably represents the activity of a shred of abnormal cortex in this region (Figure VIII).

Comment.—Both these cases are essentially the same, in that they illustrate abnormal epileptogenic activity of atrophic cortex. Case V is linked with Cases I and II, as it also illustrates amplitude asymmetry.

Theta Rhythm.

So far we have discussed the localization of cerebral lesions by the absence of normal rhythms and by the local presence of abnormal rhythms. Earlier mention was made of the θ band of frequencies—that is, those lying between four and seven cycles per second. Activity in this frequency band is most commonly seen in epilepsy; but recently Walter and Dovey[10] have produced evidence suggesting that θ activity may be characteristic of thalamic lesions. If θ rhythms are prominent and if the clinical signs of intracranial neoplasm are present, it may be inferred that the neoplasm is in the region of the thalamus. Dawson and Walter[11] have also shown that in the electro-

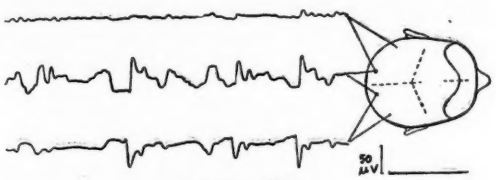

FIGURE VIII.

Case VI. "Spikes" and sharp-fronted slower waves are seen in phase reversal in the lower two tracings and have their origin in the right occipital pole. Some traces of α rhythm are seen on the left side, but on the right there is none. Compare with Figures II and III.

encephalograph a number of different frequencies are present, and that one can mask another so that it is not visible in the ordinary record. To overcome this, Walter has developed a complex and ingenious frequency analyser; this can clearly record rhythms which, to the eye, are obscured by others. However, in some cases θ rhythm is very prominent, even without the use of the frequency analyser. The final case is one of this type.

CASE VII.—A male patient, aged forty-seven years, had a history of numbness and weakness of the right side with headaches and diplopia, of three months' duration. Clinical examination revealed bilateral papillœdema, failure of upward eye movement, weakness of the right side of the face and paralysis of the right arm and leg. The cerebro-

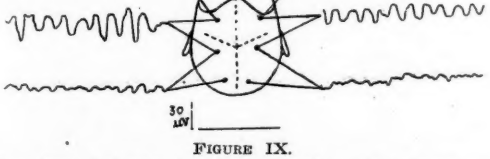

FIGURE IX.

Case VII: θ rhythm in a case of subcortical tumour. A prominent five or six cycles per second rhythm is seen in the centre tracing on each side; it is more prominent on the left. See text for details.

spinal fluid pressure was 280 millimetres of water. The electroencephalogram showed a striking θ rhythm, maximal from the pre-central and post-central placements on both sides, but more pronounced on the left side; this suggested greater involvement of the left side by a deeply placed lesion.

The post-mortem examination revealed a spongioblastoma arising in the mid-brain and invading the thalamus on each side. To the naked eye the involvement of both sides appeared to be equal; but the clinical and electroencephalographic findings suggested that greater impairment of function occurred in the left half of the thalamus.

Conclusion.

From the foregoing it might be concluded that electroencephalography is the method of choice in the localization of cerebral tumours. However, it must be emphasized that clinical examination and air studies are still pre-eminent and that the correct place of electroencephalography is as a non-traumatic aid to diagnosis.

However, the electroencephalogram is required for the detection of the epileptogenic focus. This, if inert, may be unmasked by subconvulsive doses of "Cardiazol". The method has been used here; but it is obvious that the number of cases in which it is useful is necessarily limited.

Summary.

1. A brief account of the technique and method of electroencephalography is given, with the findings in normal subjects.

2. The principles of localization of cerebral lesions by (*a*) amplitude asymmetry, (*b*) phase reversals and (*c*) detection of abnormal rhythms characteristic of lesions in certain cerebral structures are stated.

3. An indication of the scope of electroencephalography in cerebral localization is given.

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PRIMARY ATYPICAL PNEUMONIA.[1]

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THIS paper is based on a study of 29 patients examined since the beginning of June, 1947.

Definition.

Primary atypical pneumonia is a form of pneumonic consolidation of unknown origin, characterized by radiological changes out of proportion to physical signs and usually running a benign and uncomplicated course.

"Virus pneumonia" and "acute pneumonitis" are commonly used synonyms.

[1] Read at the Devon Public Hospital on November 11, 1947.

Ætiology.

The condition is thought to be a virus infection analogous to acute pneumonitis complicating certain virus infections such as influenza and measles and certain rickettsial infections such as "Q" fever.

The disease may be sporadic or epidemic, and is thought to be spread by direct contact or by droplet infection. The incubation period is usually stated to be one to three weeks; this could not be confirmed.

The cases were associated with a widespread epidemic of febrile catarrh, the incubation period of which was usually one or two days. The symptoms of febrile catarrh and of primary atypical pneumonia are similar. Only a small proportion of febrile catarrh patients were investigated radiologically; these were the patients with severe infections and those in whom some diagnostic problem required investigation; in this selected group the majority showed radiological evidence of primary atypical pneumonia.

On the other hand, during the epidemic nearly 500 patients had chest films taken for some unrelated purpose, such as routine antenatal examinations; doubtless many of these patients were suffering from less severe grades of febrile catarrh at the time of examination. In this group only one case of primary atypical pneumonia was found.

Probably primary atypical pneumonia is a part of the syndrome of febrile catarrh, developing only when the bronchioles are predominantly affected.

Immunity acquired as a result of an attack is probably short-lived. Two of the patients had been treated previously for primary atypical pneumonia of the sporadic type, one four years and one eighteen months previously. However, there is no direct evidence that the infecting agent was the same. Two children from one family suffered from primary atypical pneumonia; the interval between the admission of the first patient to hospital and the onset of symptoms in the second patient was sixty-nine days. Any immunity developed by the second child as a result of contact with the first child's infection had disappeared in little more than two months.

Pathology.

The disease is rarely fatal, but a few autopsy records have been published. The basic lesion is acute bronchiolitis, distributed focally; the bronchioles are often filled with pus, but the alveoli are often free from exudate.

Symptoms.

The symptoms are those of an acute upper respiratory tract infection; there is great variation in severity from mild coryza to severe pneumonic infection of long duration.

The ages of the patients ranged from sixteen months to seventy-five years; the incidence was highest in children aged under ten years and in middle age. The numbers of male and of female patients were nearly equal.

The onset was usually insidious, but in four cases it was sudden.

Fever was usual, but in five cases the temperature was normal throughout the period of observation. The duration of fever varied from a few hours to two months in two cases. Fall by lysis was usual, but a crisis occurred in eight cases.

Headache, malaise and cough with sputum were the most common symptoms. The cough is often "squashy" in quality, and the quantity of sputum might increase as the disease progressed. Blood-stained sputum was noted in six cases.

Dyspnœa was unusual, it occurred in six cases. Dry pharyngitis with huskiness was not uncommon. Shivering and sweating occurred in nine cases.

Aches and pains were common, varying in severity from mild discomfort to moderately severe pain. Pleuritic pain was unusual, but occurred in three patients, in one of whom a pleural friction rub could be heard on auscultation.

Abdominal symptoms present in four cases were pain, nausea and vomiting lasting for several days and sufficiently severe to cause anxiety as to the likelihood of an intraperitoneal surgical lesion. In two cases loin pains were so severe that the possibility of a surgical renal lesion had to be considered. A period of observation made the nature of the symptoms obvious.

Signs.

Pulmonary physical signs are often absent but great variation is found. Classical signs of consolidation were present in only three cases of the series under discussion, but some physical signs were detected in 19 cases, often developing after some days of observation.

Impaired percussion note was found in 11 cases, and altered breath sounds were heard in 12 cases and adventitiæ in 14 cases. *Herpes labialis* was present in one patient. Working of the *ali nasi* was not noted. The white cell counts were normal in those patients in whom continued fever suggested the possibility of suppuration.

Radiological Findings.

Radiological changes in the lungs are characteristic of the disease, and in the majority of cases the diagnosis of primary atypical pneumonia could not be made without radiology.

Distribution of the changes in the lungs follows the pattern of pneumococcal infections, being most common in one lung, as in 25 cases (usually occurring in the right lung, as in 16 cases), and most often found in the lower lobe of either lung, as in 15 cases. The shadows may be patchy in distribution, or a large part or the whole of one or more lobes may be involved.

The earliest change is an increase of striations in the affected area of lung field; in two patients no further changes developed. More advanced changes are woolly opacities, discrete or confluent, as in 15 cases. In seven cases a homogenous opacity of varying density was found. A mixture of these types was present in five cases.

The hilar glands were enlarged in 26 cases. A small pleural effusion was seen in 11 cases.

With resolution the lung fields return to a normal appearance, signs of fluid disappear and enlarged hilar glands become smaller.

Two patients had suffered previously from sporadic primary atypical pneumonia; in one the upper lobe of the right lung was affected on each occasion, in the other the upper lobe of the right lung was affected in the sporadic attack and the lower lobe of the right lung in the epidemic attack.

Course.

There were no deaths. The course of the disease is as variable as other features.

Most of the cases were of little severity, and the patients stayed in hospital for an average period of ten days; three moderately severely affected patients had an average stay of nineteen days, but in three severe cases the average stay was sixty days.

Disappearance of radiological changes in two or three weeks was usual in mild cases, but after eight weeks and ten weeks two of the severely affected patients still showed obvious changes.

Empyema and bronchiectasis have been reported as complications. None of the patients have developed any complications, but two severely affected patients were under observation for some time.

Diagnosis.

There are no specific diagnostic tests. Sporadic cases are diagnosed by excluding the presence of other disease processes and by following the course of the disease to resolution.

Sporadic cases have been comparatively few, and have usually led to a tentative diagnosis of acute pulmonary tuberculosis. In all the condition proceeded to resolution within one or two weeks.

During an epidemic the need for care lies in the opposite direction.

Difficulty was experienced in assessing the relative importance of signs and symptoms due to primary atypical pneumonia and those due to circulatory failure in three

patients who presented cardiac enlargement. In each case too little importance was attached to the primary atypical pneumonia, and consequently too serious a view was taken of the gravity of the cardiac lesion. The response of the patient to digitalis and mercurial diuretics was a valuable guide; lack of response was an indication that the signs and symptoms were largely due to the primary atypical pneumonia.

In these cases dyspnœa was distressing, and, unlike the other cases, in which dyspnœa was absent or transient, it persisted for one to three weeks. With resolution of the primary atypical pneumonia, dyspnœa subsided and reassessment of the cardiac condition allowed a happier prognosis. This was particularly gratifying in the case of a woman, aged forty-seven years, who was twenty-six weeks pregnant on her admission to hospital and who appeared to present a hopeless medical and obstetric problem.

Treatment.

Treatment consists of nursing care and symptomatic medical treatment. Published reports that the sulphonamides are of no value in treatment of this disease were confirmed. Penicillin administered by intramuscular injection or by inhalation was found to be ineffective in this condition.

Summary.

1. An account of an epidemic of primary atypical pneumonia is given.

2. The ætiology of primary atypical pneumonia is discussed.

3. A description is given of the signs, symptoms, radiological findings and course of the disease in this epidemic.

4. The diagnosis and treatment of primary atypical pneumonia are discussed.

SOME OBSERVATIONS ON THE ROLE OF PENICILLIN IN THE TREATMENT OF HÆMOPHILUS INFLUENZÆ MENINGITIS.

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THE knowledge that the hæmophilus group of organisms is relatively resistant to penicillin has until recently discouraged investigations into the possible value of penicillin in the treatment of *Hæmophilus influenzæ* meningitis. In the last two years papers have been published by Gordon and Zinnemann[1] and by North, Wilson and Anderson,[2] demonstrating the range of penicillin sensitivity of *Hæmophilus influenzæ*, with particular reference to the type B strains associated with meningitis, while a number of reports have appeared of clinical success with penicillin therapy.[3][4][5] The information given in these reports, while generally favourable, remains incomplete from the point of view of establishing a sound theoretical basis for the use of penicillin. Clinically the number of recoveries, especially of children under the age of two years, is still small, bacteriologically there is considerable confusion as to the degree of susceptibility of the organisms, and therapeutically there is uncertainty as to adequate dosage.

In Australia *Hæmophilus influenzæ* meningitis has been treated for some years with a combination of sulphonamides and immune rabbit serum, and the results, although strikingly good in comparison with previous therapy, still show a mortality rate of over 40%. In this hospital penicillin has recently been added to these methods of treatment, and in view of the limited information available it was thought desirable to institute some form of bacteriological evaluation of its usefulness in this disease.

In this investigation an attempt has been made to relate the penicillin sensitivity of the organism to the concentration of penicillin in the cerebro-spinal fluid and to arrive at a system of dosage which would ensure adequate bacteriostasis.

Methods and Materials.

Strains.

All strains tested were obtained from cultures of cerebro-spinal fluid from patients suffering from meningitis admitted to hospital during the winter and spring of 1947. All were *Hæmophilus influenzæ* type B, giving agglutination and precipitin reactions with the specific rabbit antiserum obtained from the Commonwealth Serum Laboratories. Cultures were isolated on Levinthal agar and subcultures made at three-day intervals on heated blood agar or Levinthal agar.

Penicillin Sensitivity Tests.

The standard penicillin adopted was the calcium salt of penicillin supplied by the Commonwealth Serum Laboratories for therapeutic use, in ampoules containing 200,000 units. When carefully diluted, this product has been found regularly to inhibit the growth of the standard sensitive staphylococcus B313 (American Type Culture Collection number 6538), at a minimum concentration of 0·031 unit per millilitre in nutrient broth. Sensitivity tests in fluid medium were carried out by preparing twofold serial dilutions of penicillin in one millilitre quantities of Levinthal broth and adding one drop of a 1:10 dilution of a twenty-four hour Levinthal broth culture of the strain to be tested. After twenty-four hours' incubation the tube containing the highest dilution of penicillin which showed no visible growth was taken as the index of sensitivity of the strain in question.

Tests on solid medium were made on Levinthal agar plates, to which penicillin had been added, immediately before they were poured, in such amounts as to give the same final concentrations as in the broth tests. Inoculation was again made with one drop from a 1:10 dilution of a twenty-four hour broth culture, and after twenty-four hours' incubation the end-point of visible growth was noted. By this method a number of strains could be tested simultaneously on the same series of plates.

In order to check the penicillin concentration in the media, each test included a titration of the penicillin used with the standard staphylococcus B313. All hæmophilus strains were tested as soon as possible after isolation from the cerebro-spinal fluid, the number of subcultures varying from one to five.

Penicillin Estimations.

Serial twofold dilutions of cerebro-spinal fluid were made in one-millilitre quantities of nutrient broth, and one drop of a 1:100 dilution of a twenty-four hour broth culture of the staphylococcus B313 was added. The highest dilution showing inhibition of visible growth after twenty-four hours' incubation was observed, and the concentration of penicillin in the original specimen was calculated on the basis of the limiting inhibition of this organism by 0·031 unit of penicillin per millilitre.

Sensitivity of Hæmophilus Influenzæ Strains to Penicillin.

There is at present some confusion about the precise range of sensitivity of strains of *Hæmophilus influenzæ* to penicillin. In the two largest series tested, Gordon and Zinnemann, using a heated blood agar plate incorporating penicillin, found that the range of inhibition of 16 type B strains extended from 0·5 unit to 5·0 units per millilitre, the majority being inhibited by 1·0 unit per millilitre, while North, Wilson and Anderson,[2] using a Levinthal agar broth method, showed that 34 of 51 strains tested were inhibited by four units per millilitre, all being inhibited by eight units per millilitre. These latter workers, however, reported that on Levinthal agar plates containing penicillin, all 51 strains grew in the presence of 20 units per millilitre. Forgacs, Hutchinson and Rewell[3] described their two strains as being sensitive to penicillin "to about the same degree as the standard Oxford strain of staphylococcus", and Gottlieb and

Forsyth,[6] on the evidence of a punch-plate test, regarded three of their four strains as insensitive to ten units of penicillin.

Table I gives the results with twelve recently isolated strains of *Hæmophilus influenzæ* obtained from consecutive cases of meningitis. All strains were inhibited by two units of penicillin per millilitre, the majority by one unit. No significant discrepancy was observed between tests made in broth and on agar. The table does not represent one experiment involving all twelve strains, but has been compiled from ten separate tests made at various times. In the case of six strains a series of three tests was carried out on sets of Levinthal agar plates made from different batches of medium and containing different samples of penicillin. In each test these strains gave the same individual growth end-points. By the inclusion of the staphylococcus B313 in every test it was possible to compare results with some degree of strictness. In one experiment, in which the staphylococcus titration showed an end-point at 0·016 unit of penicillin per millilitre instead of at the expected 0·031 unit, the *Hæmophilus influenzæ* end-points were correspondingly lower than in previous tests, the source of error almost certainly being faulty dilution of the penicillin. This result was discarded and the experiment was repeated with fresh dilutions of penicillin to give the correct titration end-point.

TABLE I.

Inhibition of Twelve Strains of Hæmophilus influenzæ *by Penicillin.*[1]

Type of Medium.	Number of Strains.	Units of Penicillin per Millilitre.					
		0·125	0·25	0·5	1·0	2·0	4·0
Levinthal broth.	1	++	+	−	−	−	−
	9	++	++	+	−	−	−
	2	++	++	++	+	−	−
Levinthal agar.	2	++	+	−	−	−	−
	9	++	++	+	−	−	−
	1	++	++	++	+	−	−

[1] The symbol "−" indicates absence of visible growth, and "+" and "++" denote degrees of visible growth.

Penicillin Concentration in the Cerebro-Spinal Fluid.

Investigations by Rammelkamp and Keefer[6] and by Cairns and his associates[7] have shown that intrathecal injection of penicillin can maintain complete bacteriostasis in the cerebro-spinal fluid for a period of twenty-four hours after injection when the organism belongs to the penicillin-sensitive group—that is, the staphylococcus, the pneumococcus, the streptococcus and the meningococcus. However, little information has been published concerning the rate of disappearance of penicillin from the cerebro-spinal fluid or the dosage required for relatively resistant organisms.

It was decided to study this point by estimating penicillin levels in the cerebro-spinal fluid of a group of patients suffering from *Hæmophilus influenzæ* meningitis who were receiving a standard intrathecal dose. Specimens of cerebro-spinal fluid were obtained at varying intervals after an intrathecal injection of 20,000 units of penicillin, and their penicillin content was titrated with the standard staphylococcus. All specimens were taken from patients whose illness was in a more or less active stage and whose ages ranged from four months to four years, the average age being just over two years. The majority received the Commonwealth Serum Laboratories' calcium penicillin, but some patients were given a sodium penicillin preparation manufactured by the Distillers Company, Limited, in England. Sulphadiazine by mouth and intramuscular injections of immune rabbit serum were also given to these children, but penicillin was not used intramuscularly.

The results of 23 estimations from 12 cases are shown graphically in Figure I, the penicillin concentrations being plotted logarithmically in order to show the range of values satisfactorily. Each point indicates the estimated level of penicillin in the cerebro-spinal fluid after a single intrathecal injection of 20,000 units. As fresh penicillin was given at the time of every lumbar puncture, it was not possible to obtain a series of estimations following one injection. Despite the variations of the numerous individual factors in the patients and the inherent inaccuracies of the method of estimation, the results show a certain degree of uniformity. An arbitrary line has been drawn which may be taken to represent the average rate of disappearance of penicillin from the cerebro-spinal fluid under the conditions of these tests. It can be seen that, with this dosage of penicillin, the level in the cerebro-spinal fluid falls to the range of sensitivity of the organism in twelve to eighteen hours and that, if such a dose was given only once a day, free bacterial multiplication would be possible for a period of six to twelve hours in each twenty-four.

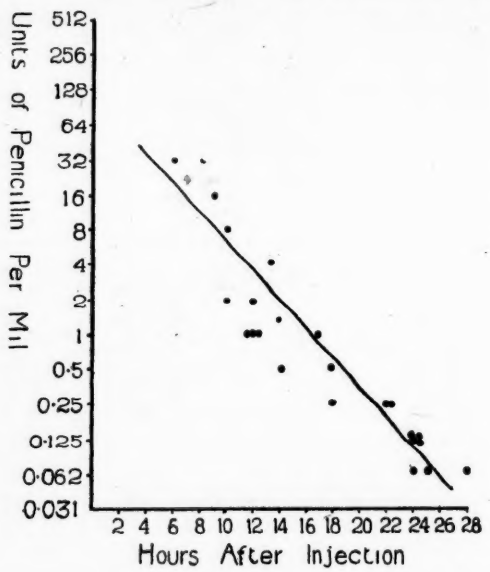

FIGURE I.

Penicillin levels in cerebro-spinal fluid after intrathecal injection of 20,000 units.

Discussion.

In their comprehensive review of the treatment of *Hæmophilus influenzæ* meningitis in Australia, North, Wilson and Anderson[8] have shown that the introduction of sulphonamides led to a reduction of the mortality rate from 98·8% to 78%, and the addition of immune rabbit serum further reduced it to 44·2%. In England, where immune rabbit serum is not available for the treatment of these patients, recoveries are being recorded among children under the age of two years with the use of penicillin and sulphonamides. The intrathecal dose recommended by English workers is 50,000 units of purified penicillin, given once a day.

If we assume that the rate of elimination of penicillin from the cerebro-spinal fluid shown in Figure I is approximately correct and independent of the initial concentration of penicillin, a dose of 50,000 units would extend the period of bacterial inhibition for only four hours and would still leave a short time each day in which multiplication could take place. The single daily dose of 20,000 units used in this hospital as a standard treatment for meningitis, while sufficient for the most sensitive organisms, is clearly inadequate from the point of view of maintaining uninterrupted bacteriostasis for a group of organisms whose sensitivity varies from 0·5 unit to 2·0 units per millilitre. If, however, injections are made at intervals of twelve instead of twenty-four hours, the concentration should not

fall below the critical level. This system of twice-daily intrathecal injections of 20,000 units has been adopted for the time being as a routine procedure in the treatment of *Hæmophilus influenzæ* meningitis, and it is thought that the maintenance of a constant inhibitory concentration justifies the trouble of additional lumbar punctures. When more highly purified preparations of penicillin are available, it may be possible to give a daily injection of 100,000 units and achieve the required concentrations for twenty-four hours. At present clinicians are unwilling to inject such concentrated solutions of commercial penicillin into the subarachnoid space, on account of the undesirable reactions which may follow.

The accurate clinical assessment of the part played by penicillin, combined as it is with sulphonamides and serum, will necessitate the accumulation of a large series of cases. Examination of the records of children who have died in spite of treatment with immune serum shows that they fall into two main groups. The first consists of young infants who are admitted to hospital in an extremely ill, often moribund, condition and die within a few hours. Post-mortem findings indicate that these infections must have been present for many days, even though symptoms and signs have been minimal or absent. The problem here is one of early diagnosis and it is unlikely that any treatment would be of use by the time the diagnosis is finally made. The other group comprises patients who at first respond well to treatment, their symptoms receding and cultures ceasing to be obtainable, only to relapse and die after a stormy course, with the reappearance of organisms in the cerebro-spinal fluid. It is in this group that the bacteriostatic power of penicillin may be of the greatest importance. Although the number of patients so far treated with penicillin in this hospital is too small to enable any conclusions to be drawn, the results can be said to be encouraging.

The number of strains available for testing in these observations has been small, and although they have shown a fairly constant degree of susceptibility, it is possible that more resistant strains will be encountered in the future. The present lack of agreement about the precise range of sensitivity of type B *Hæmophilus influenzæ* strains would appear to have arisen from variations in the materials and techniques employed for testing. By the inclusion of the standard staphylococcus B313 as a reference organism in all tests of this investigation it has been possible to establish a direct relationship between sensitivity of the organisms and penicillin concentrations in the cerebro-spinal fluid, which is independent of the calculations based on the stated quantities of penicillin in the samples used.

It seems probable that streptomycin will become the antibiotic of choice in the treatment of *Hæmophilus influenzæ* meningitis. Alexander, Leidy, Rake and Donovick[9] have already shown its efficacy, and further reports will doubtless be published shortly. However, there are at present several factors to be considered in connexion with streptomycin. These include shortage of supplies, cost, toxicity, and the readiness, in some cases, with which organisms can acquire a high degree of resistance during treatment. Until these difficulties are overcome and the position of streptomycin is firmly established, penicillin is likely to be of considerable value.

Summary.

1. Twelve strains of type B *Hæmophilus influenzæ* show penicillin sensitivities in the range of 0·5 unit to 2·0 units per millilitre.

2. Estimations of penicillin in the cerebro-spinal fluid of patients with *Hæmophilus influenzæ* meningitis receiving a daily intrathecal injection of 20,000 units of penicillin show that an inhibitory level for these organisms is maintained only for a period of twelve to eighteen hours.

3. It is suggested that intrathecal injections of 20,000 units of penicillin, spaced at intervals of twelve hours, could provide an adequate and continuous bacteriostatic concentration in the cerebro-spinal fluid and thus form a useful addition to the existing methods of treatment.

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THE OCCURRENCE OF RAPID POTENTIAL CHANGES IN THE ELECTROENCEPHALOGRAM.[1]

By M. H. Draper, R. S. Edgar and W. A. Dibden,[2]

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The variations of electrical potential associated with the activity of the brain and recorded from electrodes placed on the scalp present in general a complex pattern of a non-repetitive nature.

Early workers in the field of electroencephalography discovered that brain waves were sometimes quasi-sinusoidal in form and roughly constant in period over short lengths of time. These observations gave rise to the names α, β and δ waves, designating respectively those quasi-sinusoidal waves with frequencies respectively of seven to fourteen cycles per second, fourteen to sixty cycles per second, and less than seven cycles per second. In these cases, in which attention is directed towards processes of non-uniform repetition rate, such as sporadic spike potentials, it becomes necessary to state the time function of the process in terms of period only. Where non-sinusoidal variations of constant repetition rate obtain (as is possible in nerve fibres), and where the significance of these changes may appear to be lost if a mathematical resolution into component sinusoidal frequencies is attempted, the variation may best be stated in terms of period and repetition rate.

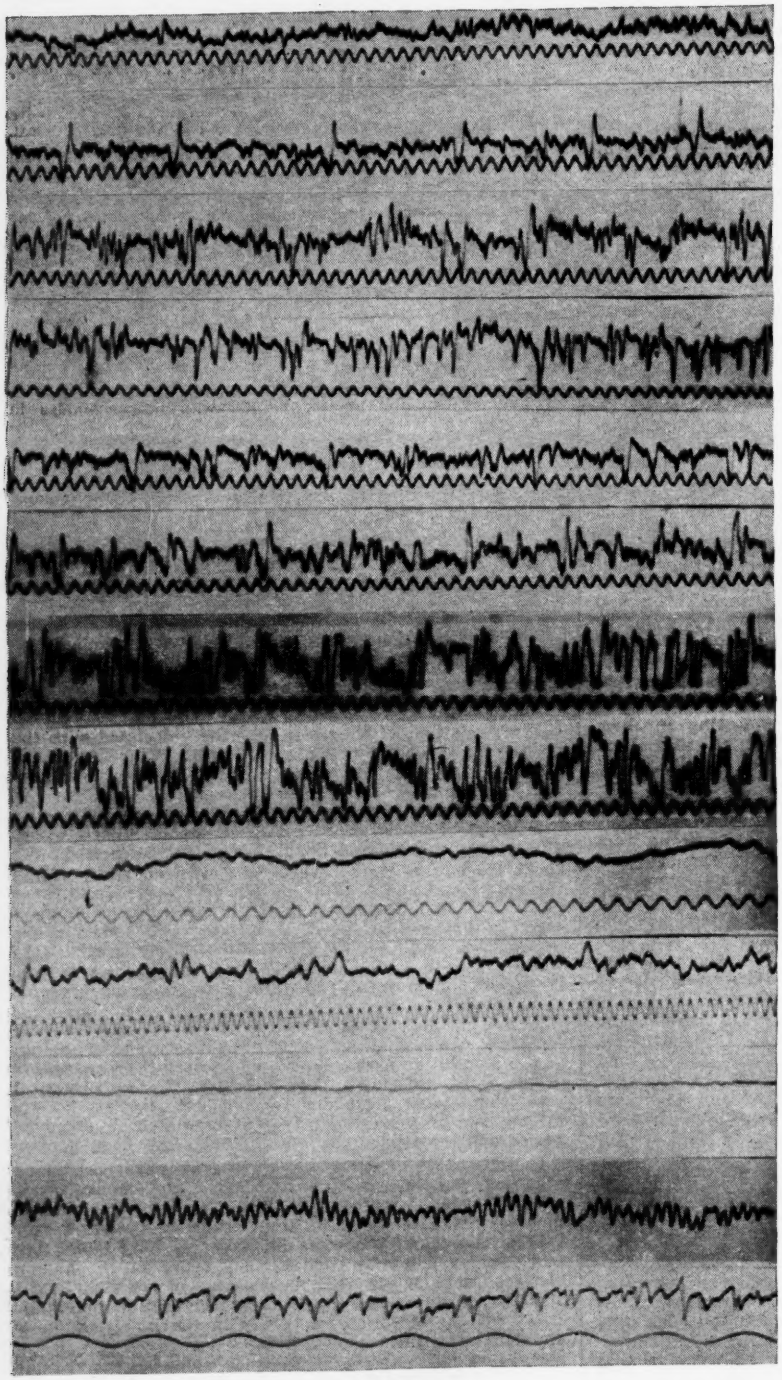
In the course of our investigations we have been using high gain amplifiers with a flat response from one cycle to 3000 cycles per second. Recordings are made on a moving photographic film from a double beam Cossor cathode ray tube. With this apparatus we have found that much faster potential changes may occur in the human electroencephalogram than those usually reported. The significance of artefacts due to muscle action potentials needs further attention, especially in the investigation of emotional patients.

The possible clinical significance of these more rapid potential changes is illustrated by the following case.

A married woman, aged thirty-seven years, fell from a moving vehicle in 1944. She suffered linear fractures in the right temporo-parietal region, and hæmorrhage from her naso-pharynx and right ear occurred. Immediately after the fall she was dazed, but not unconscious. The next

[1] Read at a meeting of the Medical Sciences Club of South Australia on October 5, 1946.

[2] The work is being carried out under grants from the National Health and Medical Research Council.



FIGURES I to VIII. Electroencephalograms taken with a wide band pass amplifier and cathode ray recording, showing the unusual tracing from a woman with uncinate fits.

FIGURES IX and X. Two representative normal tracings.

FIGURE XI. Showing the noise level of the amplifying system under higher amplification than was used for the previous tracings. The calibration in all these tracings is a 100-cycle wave. The appearance of the electroencephalogram of the same person as in Figure IX, with all the frequencies above 50 filtered out, is shown in Figure XII, which represents eight seconds of tracing. This is the equivalent of the usual penwriter performance.

FIGURE XIII. This tracing has a 50-cycle wave for calibration and is taken from the unexposed brain of a rat.

morning she was found unconscious, and was admitted to hospital for observation. She was discharged thirteen days later, apparently well. Subsequently she became alcoholic and began to suffer from true epileptiform seizures. She had an aura of a bad smell and taste suggesting an uncinate fit. Recent clinical examination revealed no abnormality apart from the fact that the left pupil was greater than the right.

Her electroencephalographic recording from the parieto-temporal region with monophasic leads showed, on the right side, slow potential changes, period 0·1 second, and superimposed on these were low voltage spikes of an average period of 0·003 second with an occasional spike of greater amplitude (Figures I and II). The recording from the left side showed a greater number of spikes, period 0·003 second, with three times the amplitude of the smaller changes (Figures III and IV). There were, on the average, about ten times the number of fast spikes on the left side. After three minutes of hyperventilation the number of high amplitude spikes increased on the right side to something approaching the normal left side record (Figures V and VI). The left side record, however, shows a threefold increase in amplitude and in the number of spikes of larger amplitude (Figures VII and VIII). The change in the records is striking. There are also evident in all the tracings from this patient potential changes of very low amplitude and of period approaching 0·001 second—that is, in the looser nomenclature usually employed, of a frequency approaching 1000 cycles per second. A subsequent pneumoencephalogram suggested a diagnosis of left cortical atrophy in the temporal region.

Figure IX is a tracing from a normal person who exhibits pronounced α rhythm at all times. Figure X is a tracing from a normal person who never has shown α rhythm, a so-called β rhythm type of tracing. These have been depicted on a similar time scale for comparison. Figure XI shows the noise level of the amplifier with a higher gain than was used for the taking of the electroencephalograms. Figure XII shows the usual form of α rhythm, recorded so as to filter out any frequency above 50 cycles per second and with a film speed of two centimetres per second.

We do not wish at this stage to draw any conclusions with regard to the occurrence

in normal or abnormal subjects of these low period potential changes; but we do suggest that more attention to their occurrence and interpretation is needed. This will necessitate the use of recording systems capable of much better frequency responses than the commonly used penwriters, and of amplifiers with wide band pass characteristics. A more accurate terminology than the hitherto used "waves" and "rhythms" would seem to be indicated if this quantitative approach to electroencephalography should prove useful.

Our own observations have led us to hope that this type of recording may be of assistance in the psychiatric and psychological spheres. Figure XIII is a recording from the unexposed brain of a rat under light "Nembutal" anæsthesia (the calibration is a 50 cycle per second wave). This shows that, in the field of neurophysiology, appreciation of the possibilities of more accurate recordings of brain potentials may have a wide application.

Study along the general lines indicated above is proceeding in Tbilin, Georgia, Union of Socialist Soviet Republics, under Professor Beritoff.[1]

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THE DIAMETER OF CARDIAC MUSCLE FIBRES: A STUDY OF THE DIAMETER OF MUSCLE FIBRES IN THE LEFT VENTRICLE IN NORMAL HEARTS AND IN THE LEFT VENTRICULAR ENLARGEMENT OF SIMPLE HYPERTENSION.

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SINCE late in the nineteenth century several workers have determined the transverse diameter of cardiac muscle fibres in both normal and hypertrophied hearts. They record average values for fibres from the full thickness of the left or right ventricular wall or the papillary muscles. In this investigation we have determined the transverse diameters of cardiac muscle fibres in each of the four major layers of the left ventricular wall in normal hearts and in hearts hypertrophied from simple hypertension.

Historical Survey.

The first measurements of cardiac muscle fibre diameters made with any degree of accuracy were those of Goldenberg (1886). He measured fibre diameters in histological sections made from several sites in both left and right ventricular walls. These sections were fixed with Müller's fluid and after dehydration embedded in celloidon for cutting. His values for the normal adult were derived from three hearts, and for left ventricular hypertrophy from five hearts.

In 1925 Karsner, Saphir and Todd measured fibre diameters in the left ventricular wall in one normal, one atrophied and one hypertrophied heart. They employed a paraffin embedding method of cutting sections.

In a series of papers in 1938 and 1941 Wearn *et alii* determined mean diameters of fibres from right and left ventricular walls in normal and hypertrophied hearts. These authors used a formalin fixation method followed by gelatin embedding.

Ashley (1945), commenting on the variation in techniques used to prepare sections by previous workers, devised a non-shrinking technique in an attempt to determine the actual size of the fibres during life. He based his determinations on an examination of fifty normal hearts.

The mean diameters determined by these workers (Table I) show considerable variation, which is probably due to the various techniques of section cutting adopted.

Methods and Material.

The hearts used in this investigation were five macroscopically normal ones from young adults (numbers 106, 114, 116, 120, 134) and two (numbers 113, 115)[1] from adults who had simple hypertension without congestive

TABLE I.

Author.	Mean Fibre Size.	Site.
Normal Hearts.		
Goldenberg ..	12·4μ	Left ventricular wall.
Karsner *et alii* ..	17·6μ	Left ventricular wall.
Wearn *et alii* ..	14·0μ	Average of right and left ventricular walls.
Ashley	(*a*) 19·5μ	Left ventricular wall.
	(*b*) 20·6μ	Left ventricular wall.
Hypertrophy of Left Ventricle.		
Goldenberg ..	15·9μ	
Karsner *et alii* ..	31·05μ	
Wearn *et alii* ..	21·0μ	

cardiac failure and who died non-cardiac deaths. These last two hearts, which weighed respectively 20 ounces (567 grammes) and 30 ounces (850 grammes) showed no gross coronary artery disease and were enlarged only in the left ventricle. All hearts after fixation appeared to be in a comparable phase of partial systole.

Histological sections in a plane parallel to the base were prepared from the lateral wall of the left ventricle at the junction of the middle and basal thirds of its length. As only comparative values between the layers were required, no attempt was made to avoid shrinkage of the material in cutting these sections. The tissues were first fixed in a 10% solution of formalin in normal saline solution for periods varying from one week to several years. They were then dehydrated in alcohols and embedded in paraffin for cutting.

It was thought that the variation in the time of fixation in formalin might affect the degree of shrinkage of the sections; but measurements made on these and other specimens indicate that complete dehydration occurs in the preparation and that the degree of shrinkage is ultimately the same, irrespective of the duration of initial formalin fixation. The final fibre sizes are considered to be comparable and shrinkage to be of the order of 15% to 20% of a linear dimension.

The sections (8·0μ thick) were studied under a magnification of 600 diameters and measured by a ruled grid placed in the microscope eyepiece. With this grid measurements could be estimated to 1·0μ.

In these sections of the ventricular wall the fibres in each layer run in different directions. As measurements were to be made on all layers, it was impossible to select only those fibres cut in true cross-section or true longitudinal section. It was assumed, therefore, that between anastomoses each fibre was cylindrical in shape, and consequently the shortest diameter in an oblique section represented the true diameter of the cylinder.

In the normal hearts 40 fibres were measured in each muscle layer and those for the five hearts were combined. In the hypertrophied hearts 200 fibres were measured in each layer.

[1] The serial numbers refer to hearts examined in these and other studies.

In all cases the fibres measured appeared normal on histological examination.

Results.

In the sections made the four major muscle layers in the left ventricular wall represent the external portion of the superficial bulbo-spiral muscle (S.B.S.), the deep sino-spiral muscle (D.S.S.), the deep bulbo-spiral muscle (D.B.S.) and the internal portion of the superficial sino-spiral muscle (S.S.S.).

The mean values obtained for the fibre diameters and their standard deviations are set out in Tables II and III. Figures I, II and III are histograms showing the frequency distributions of fibre diameters in the various muscles of the ventricular wall.

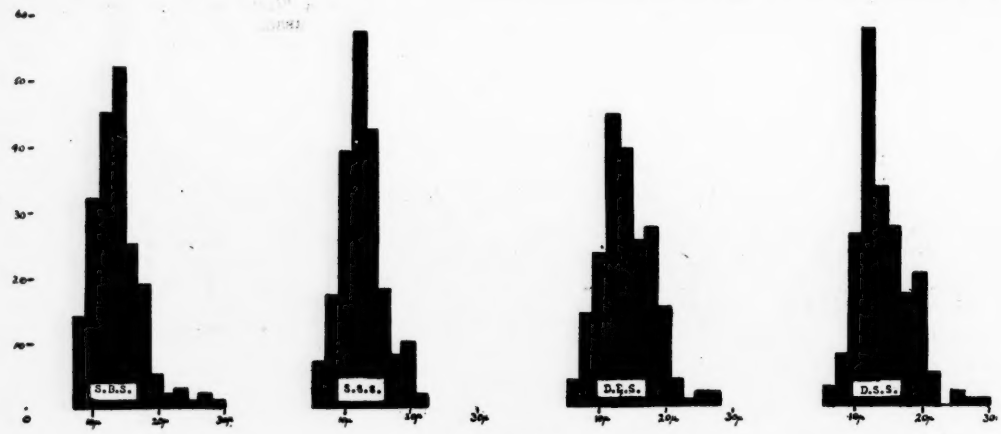

FIGURE I.
Normal hearts. Histograms showing frequency of distribution of fibre diameters in each muscle.

Table II and Figure I show that in the normal heart there is only a small variation in fibre size and that the distribution of fibres of various sizes is symmetrical about the mean. There is also marked uniformity between the three outer layers, but the mean value for the inner layer is significantly smaller than that for the others.

Table III and Figures II and III show that in the hypertrophied hearts there are enlargement of fibres and increase in the range of fibre size, and the distribution of fibre size about the mean is symmetrical. In contrast to the observations in the normal hearts the mean fibre size in the internal layer is not significantly different from that in other layers.

It is also noted that although hearts numbers 113 and 115 were considerably different in weight, the mean values of their fibre sizes were the same.

TABLE II.
Normal Hearts.

Layers.	Mean Fibre Diameter.	Standard Deviation.
S.B.S. (external) ..	13·6μ	±1·85μ
D.S.S.	13·6μ	±1·94μ
D.B.S.	14·0μ	±1·95μ
S.S.S. (internal) ..	12·5μ	±1·57μ

Commentary.

In considering the metabolic problems of hypertrophied fibres, both Harrison (1935) and Wearn (1941) concluded that there must be a maximum diameter for these fibres beyond which cellular nutrition, dependent on the diffusion of metabolites to and from adjacent capillaries, could not function efficiently. Harrison placed this maximum diameter in the region of 25μ.

In contrast to the results recorded here and also to those of Goldenberg, Karsner and his co-workers found that their measurements of fibre diameters in an hypertrophied heart were not symmetrically distributed about the mean, but were skewed towards the larger fibre sizes. They concluded that this indicated that when fibre hypertrophy occurred all fibres tended to approach a uniform maximum diameter and referred to this maximum as a "limit of hypertrophy".

Our observations on hypertensive hearts show that there is uniformity of the mean diameter of the enlarged fibres in all layers of the wall and that a similar degree of hypertrophy has occurred in each layer. That this uniformity may not be a universal feature in all hypertrophied hearts is indicated by the macroscopic measurements of the layer thicknesses made by Robb (1938), who found that the deep bulbo-spiral muscle was often differentially thickened. If Karsner's results are reconsidered in the light of this observation, it is possible that the skew distribution of fibre sizes, which he noted, indicates not an approach of all fibres to a "limit of hypertrophy", but the dominance in his results of fibres from one layer in which hypertrophy was much greater than in the remainder of the wall. His selection for measurement only of fibres cut longitudinally would permit such a layer effect to occur.

TABLE III.
Hypertrophy of Left Ventricle.

Layers.	Heart Number.	Mean Fibre Diameter.	Standard Deviation.
S.B.S. (external) ..	113	20·4μ	±5·65μ
	115	20·3μ	±6·9μ
D.S.S.	113	21·0μ	±6·4μ
	115	21·5μ	±7·0μ
D.B.S.	113	21·1μ	±6·8μ
	115	22·3μ	±7·5μ
S.S.S. (internal) ..	113	21·0μ	±6·5μ
	115	21·6μ	±6·1μ

Despite doubt as to the validity of the conclusions of Karsner *et alii*, several methods of approach already considered suggest that there is a "limit of hypertrophy" of cardiac muscle fibres. This concept gives a ready explanation of the observation that the mean fibre size and distribution of fibre size in the two hypertrophied hearts examined here are almost identical, despite the marked difference in their weights. It suggests that they have both reached the "limit of hypertrophy". If allowance is made for the differences in the techniques of section cutting, our value of 21μ (approximately) for the mean diameter of the hypertrophied fibres agrees well with Harrison's theoretical maximum value of 25μ for the "limit of hypertrophy".

The marked difference in the weights of the hypertrophied hearts with the same fibre diameters shows that, in itself, heart weight is not necessarily a good index of the degree of muscle hypertrophy. In these hearts there is no microscopic evidence to suggest hyperplasia of fibres; but this possibility is not excluded, for hyperplasia might have occurred at some distant time and the muscle be now in a stable state. Further, Karsner has indicated that the total number of fibres in different hearts is approximately the same. The differences in weight must therefore be due to alterations in the amounts of interstitial fluid or tissue.

If the tension which a muscle fibre can develop is proportional to its cross-sectional area (Harrison), then in each of the hearts examined a striking uniformity of tension in the muscle layers of the left ventricle can be deduced. In the hypertrophied hearts the mean cross-sectional area of the fibres in each layer is the same. In the normal hearts, however, the mean cross-sectional areas of fibres, whilst uniform in the outer layers, are slightly but significantly less in the innermost layer. These observations imply therefore that in the normal heart the tensions are uniform in the outer three layers and slightly less in the innermost layers. In the hypertrophied hearts the tension seems to be uniform in all layers.

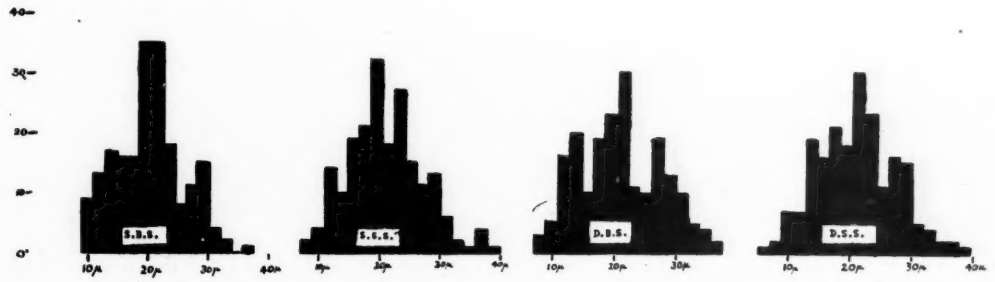

FIGURE II.

Simple hypertension (heart 113). Histograms showing frequency distribution of fibre diameters in each muscle.

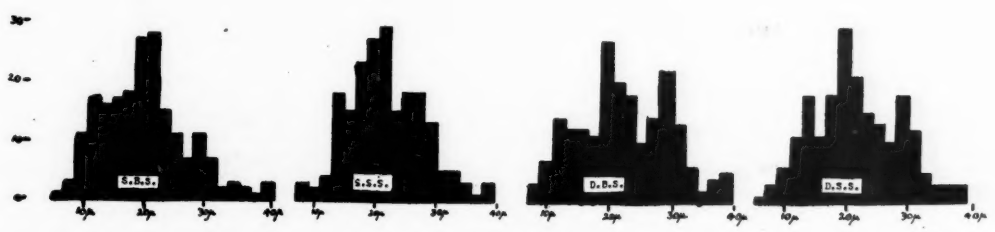

FIGURE III.

Simple hypertension (heart 115). Histograms showing frequency distribution of fibre diameters in each muscle.

Conclusions.

The results presented here lead to two conclusions relating to the hearts examined. Firstly, the uniformity of fibre size in the hypertrophied hearts provides additional evidence for the concept of a "limit of hypertrophy" for cardiac muscle fibres. Secondly, there is uniform hypertrophy in each muscle layer of the enlarged hearts.

The results also indicate that in the hypertrophied hearts there is uniformity of tension in each muscle layer, and that in the normal hearts, whilst tension seems to be uniform in the outer layers, it is perhaps slightly less in the innermost layer of the left ventricular wall.

Summary.

1. The mean diameters of cardiac muscle fibres of the left ventricular wall of five normal hearts and two hearts with left ventricular hypertrophy are recorded, and grouped according to cardiac muscles.

2. The concept of a "limit of hypertrophy" for cardiac muscle fibres is discussed and supported by arguments arising from the measurements made.

3. The tensions in the various layers of the left ventricular wall are considered to be uniform in the hypertrophied hearts. In the normal hearts tension is thought to be slightly lower in the innermost layer of the ventricular wall.

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Reports of Cases.

ACUTE SUPPURATIVE CHOLANGITIS WITH RECOVERY AFTER THE USE OF PENICILLIN AND STREPTOMYCIN.

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On July 16, 1947, J.Y., aged thirty-eight years, a motor truck driver, was admitted to hospital suffering from biliary colic of thirty-six hours' duration. On examination the patient was found to be deeply jaundiced, with hyperæsthesia, tenderness and guarding in the right hypochondrium. The lung bases, however, were clear. Intermittent attacks of varying severity had occurred during the last two years, with one previous episode of jaundice early in 1946. On this account he had been admitted to a suburban hospital but had left before any treatment was commenced. In the three weeks prior to his admission to hospital on July 16, 1947, the patient had suffered from recurring bouts of biliary colic, and in this time he had noticed that his urine was occasionally dark in colour and that his stools were pale and bulky.

On his admission to hospital the patient was given great relief by an injection of morphine (one-quarter of a grain) and atropine (one seventy-fifth of a grain). The next morning he had a slight rigor at 7 a.m. and a severe rigor at 11 a.m. The temperature fell during the afternoon and the general condition appeared to improve. During the following morning two more severe rigors occurred and the patient became irrational and non-cooperative, so that the intravenous administration of glucose and saline solution had to be discontinued.

Operation was deemed essential during the afternoon, and a large stone was felt impacted in the common bile duct behind the pylorus; it was oval in shape, three-quarters of an inch long and one-quarter of an inch in its widest diameter. On palpation the gall-bladder was hard and fibrotic but contained no stones. The common duct was opened and there was an immediate rush of white bile and creamy pus, estimated to be about half a pint in volume; more of this fluid flowed from the duct when the left lobe of the liver was squeezed. The liver itself was a dull crimson colour with many small pin-point areas of infected white bile. Cholecystostomy and choledochostomy were performed under cyclopropane and oxygen anæsthesia with curare (15 milligrammes of "Tubocurarine"). Streptomycin treatment was commenced on the patient's arrival back in the ward, as the invader was considered to be most probably a Gram-negative organism.

After operation the patient's condition rapidly improved. Bile began to drain after twelve hours, and convalescence was uneventful except for a slight rigor on the seventh day and a short rise in temperature to 102° F. on the ninth day. The patient was discharged from hospital on the twenty-fourth day, his pulse rate and temperature having been normal for twelve days and the patient himself feeling very well. Clinical follow-up investigations for three months after operation show that the patient has been in excellent health since his discharge from hospital.

Repeated cultural examination of the bile taken at operation and of the normal bile secreted from the day after operation failed to reveal the causative organism.

Streptomycin was prepared by dissolving one gramme in 10 millilitres of normal saline solution, and two millilitres were given every three hours for a course of 20 grammes. Two million units of penicillin were administered concurrently and during convalescence the patient had a daily diet of 5000 Calories containing 300 grammes of protein.

Comment.

The recovery rate from suppurative cholangitis associated with multiple liver abscesses is not high, and the report of this case, in which deterioration progressed despite pre-operative administration of penicillin, may be of interest. It is thought that the administration of streptomycin contributed greatly to the successful result.

Reviews.

DE LEE'S OBSTETRICS.

The appearance of the ninth edition of De Lee's "Principles and Practice of Obstetrics" will be welcomed by students and by all practitioners who are interested in the art of obstetrics.[1] Since its first appearance in 1913 this has been a classic among textbooks and the previous high standard is still maintained. This last edition has been revised and largely rewritten by Greenhill, who assisted in earlier editions.

The whole field of obstetrics is covered and all accepted methods of treatment are discussed. One valuable and unusual feature is the full list of references to original articles which is placed at the end of each chapter. Fresh knowledge of fœtal physiology has necessitated a new section on this subject, and the former chapters on ante-partum care and post-partum care have also been replaced by new ones. The separate grouping of minor disturbances of pregnancy is useful. The section on analgesia and anæsthesia contains much new material; it gives an excellent survey of all methods in present-day use with a full description of the newer methods of caudal analgesia and parasacral block; the importance of the establishment of confidence and of the removal of fears is recognized. Modern chemotherapy for puerperal infections receives adequate attention, but it seems strange that lysol and biniodide of mercury should still be recommended as antiseptics for the vulva and vagina when better and proven preparations are available. *Erythroblastosis fœtalis* is briefly discussed in a new chapter. The book is well illustrated and can be thoroughly recommended both as a textbook and as a work of reference.

GYNÆCOLOGY.

"Progress in Gynecology", edited by Meigs and Sturgis, is a collection of papers on gynæcological subjects[2] by seventy-one authors each discussing his own "hobby". Naturally there is a marked variation in standard, but every aspect of gynæcology is covered. The editors acknowledge the overlap of discussion which occasionally occurs and the fact that references are cut to a minimum. In parts there is not enough differentiation made between old ideas and modern advances. The book is very well set out and the paper is good.

Schiller describes a congenital "erosion" of the cervix as arising from a failure of squamous cloacal epithelium to grow upwards over the external os. He does not state whether this theory is original or from what source it is derived. It is, however, in distinct contrast to the universally accepted view championed by Robert Meyer that the columnar epithelium grows down over the squamous epithelium.

Clear reviews of present knowledge concerning menstruation are given by those most intimately connected with recent researches into the problem. There is an excellent chapter by Sturgis on amenorrhœa, the classification into uterine, ovarian, pituitary and hypothalamic types being much more acceptable than the old primary and secondary groupings. Hamblen's statement that thyreoid extract in the treatment of functional uterine bleeding is of no value unless the patient is hypothyreoid is not in keeping with clinical experience. By many gynæcologists it is found to be one of the most valuable forms of endocrine therapy when used quite empirically. In a satisfactory chapter on dysmenorrhœa Ingersoll rightly gives a warning of a possible psychoneurotic basis. There is a valuable chapter on

[1] "Principles and Practice of Obstetrics", by Joseph B. De Lee, M.D., and J. P. Greenhill, M.D.; Ninth Edition; 1947. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 7", pp. 1022, with many illustrations, some of them coloured. Price: 75s.

[2] "Progress in Gynecology", edited by Joe V. Meigs, M.D., and Somers H. Sturgis, M.D.; 1947. London: William Heinemann (Medical Books), Limited. 9" × 6", pp. 566, with many illustrations, some of them coloured. Price: 35s.

androgen therapy which details present knowledge on the subject.

It is rather surprising to find Simmons advocating the use of air for Rubin's tests and lipiodol for hysterosalpingography without any mention of the respective dangers of air embolism or foreign body granulomata. An excellent chapter by Eastman on habitual abortion gives a balanced assessment of the value of known types of therapy. It is astounding to find Everett and Kleegman both remarking on the non-occurrence of trichomonas vaginitis in young children. Clinically it is a by no means uncommon finding if a careful search is made for the protozoon. Of great interest is the reference to the treatment of chronic cervicitis by quick freezing with the use of special electrodes, the apparatus working on the same principle as the refrigerator. No mention is made of the use of chemical cauterization or of the possible hormonal relationship to the ætiology of cervicitis.

In a discussion on miscarriage and septic abortion Lynch states that in the last trimester or at full term, if the fœtus is dead, the uterus should be emptied or well-known consequences leading to sepsis eventuate. This is a dangerous statement which may lead the reader to empty the uterus by surgical means. In actual practice these untoward consequences occur as a rule only as a result of interference, and as long as the membranes are intact the patient is not in any danger. There is a very good chapter by Holmes on endometriosis.

Randall has presented a logical survey of adenocarcinoma of the uterus and its treatment. A comprehensive survey is given of carcinoma of the cervix, including every known method of treatment of the local lesions and lymphatic metastases. Montgomery describes his preparation of the vagina for the Manchester-Fothergill operation, using soap solution and 1 in 1000 "Zephiran" solution. It should be pointed out, however, that "Zephiran" is incompatible therapeutically with soap and the latter should be very carefully removed before the "Zephiran" is applied.

There is still some confused thinking about streptococci and their relation to infections. Lyons refers to hæmolytic streptococci which aerobic cultures fail to identify. It would be wiser to differentiate between hæmolytic streptococci and anaerobic streptococci. The latter can be found on anaerobic culture, but they must be searched for carefully. In the same chapter some new ideas are presented in that to "gross surgical pathology of the wound is assigned greater importance" than the older conception of choosing "chemotherapy solely on the basis of bacteriologic identity of the infecting organism". Keeger states that in tests of cure for gonococcal infections "all patients should be followed by both smears and bacteriologic cultures for at least two weeks before a cure is accepted". Surely two weeks should read twelve weeks, as few experts in venereal disease would discharge a patient in under two to three months. There is an interesting table showing the relative incidence of different bacteria in puerperal sepsis. The largest group is the unknown group, followed by a much smaller percentage of hæmolytic streptococci and anaerobic streptococci. Clinically one finds that the more frequent organism is the anaerobic streptococcus, which, of course has to be searched for in anaerobic cultures. The above figures suggest inadequate laboratory investigation.

The editors intended that this book should refresh the minds of those returning to practice after the war, and this object should be fully realized in a book so admirably presented.

A REVELATION OF BENJAMIN RUSH.

FOR some strange and unaccountable reason the Philosophical Library of New York has seen fit to publish a book of 433 pages, "The Selected Writings of Benjamin Rush", edited by Dagobert D. Runes.[1] In a preface eulogistic of the author of these writings, we are told that he was born near Philadelphia in 1745, that he received the "bachelor's degree" from Princeton College at the age of fifteen, was then apprenticed to a Dr. Redman for six years, and, in 1768, was awarded the degree of Doctor of Medicine from the University of Edinburgh. Returning to his native city after a short visit to France, he was appointed Professor of Chemistry in the College of Philadelphia in 1769. When, in 1791, the same college achieved the higher status of a university, he became Professor of the Institutes and Practices of Medicine.

Since those halcyon days of wild speculation and blind empiricism in the principles and practice of medicine, Benjamin Rush has been periodically hailed with more or less enthusiasm as the "father of American medicine" or as the "American Hippocrates". He was undoubtedly a great American patriot and is entitled to fame as one of the signatories of the Declaration of Independence, but a careful perusal of his writings as presented in this book will quickly dispel any illusion that he was ever a great doctor, or even a great thinker. There is much to be said for a movement to resurrect the works of some of the ancients who have added ever so little to human knowledge; but the nonsense contained within the pages of this twentieth century production will do nothing more than convince the intelligent reader that Dr. Benjamin Rush was an unimportant product of his times.

It is difficult to understand the attitude of such eminent medical historians as John Shaw Billings and William H. Welch, who, apparently, were able to discover some virtue in the philosophy of Benjamin Rush, and while we think that their opinions must be treated with respect, we also think that the sooner Rush is forgotten the better.

SURGERY FOR STUDENTS.

A SECOND edition of Pannett's book on surgery shows little change from the first.[1] It still features very clear line illustrations of anatomy and surgery and a lucid "Anglo-Saxon" English style of prose. The diagrams of X-ray pictures have all been transferred from positive to negative, so as to approximate more closely to the skiagrams which they are intended to portray. Of particular note are the illustrations of the types of fractures and of the modes of violence causing them. Line drawings depict the more common techniques of treatment. While many recent advances are omitted, a basis of surgery is adequately presented.

The book is intended to give a student the groundwork of "the bones" of surgery: a minor criticism of a book which should be useful to the undergraduate student is that in this "surgical osteology" descriptions of fossils are still to be found.

"PSYCHOPATHOLOGY."

IT is interesting to note the arrival of a fourth edition of "Psychopathology" by J. Ernest Nicole.[2] First printed in 1930, the work is an outstanding success. It gives in concise form a survey of modern approaches to the field of psychiatry. The author admits that only a few additions have proved necessary, so that the book differs only in detail from its predecessor.

Dr. Nicole is to be congratulated on his wide viewpoint; after dealing with that of the classical authors Morton Prince, Freud, Adler, Jung and Rivers, he has chapters on endocrine theories, biochemical findings, and other physiological and anatomical contributions.

A section is devoted to the constitutional approach of Kretschmer. This is followed by a study in ethnology and sociology, which includes a wide variety of aspects. It includes the work of Malinowski and Mead in the Trobriand Islands and suggests that freedom from neurosis is attributed to sexual freedom during childhood and adolescence with elimination of the concept of sex as sinful. Davis's analysis of 2200 women, among whom of 1200 50% admitted homosexual tendencies, is also mentioned.

In a chapter on the eclectics and characterologists the author classifies the main psychological theories. He admits the need for correlating the schools of thought, but realizes that to date attempts on these lines have "resulted not so much in a unification as in a mere combination". After reading "Psychopathology", the reader has a vivid realization of the amazing amount of work in many fields. The references are factual and unbiased; no individual school receives the limelight. We are left with a surfeit of riches, which though humbling our pride by realization of our ignorance, results in a feeling of frustration. It is difficult

[1] "The Selected Writings of Benjamin Rush", edited by Dagobert D. Runes; 1947. New York: Philosophical Library. 8" x 5½", pp. 448. Price: $5.00.

[1] "Surgery: A Textbook for Students", by Charles Aubrey Pannett, B.Sc., M.D., F.R.C.S.; Second Edition; 1947. London: Hodder and Stoughton, Limited. 9¾" x 6¼", pp. 782, with many illustrations. Price: 27s. 6d.

[2] "Psychopathology: A Survey of Modern Approaches", by J. Ernest Nicole, O.B.E., L.M.S.S.A., D.P.M.R.C.P. and S.; Fourth Edition; 1946. London: Baillière, Tindall and Cox. 8½" x 5½", pp. 278. Price: 15s.

to digest the rich meats at this intellectual table. In a future edition it is to be hoped that the author will have the temerity to cull some of his authorities and give more leads to the probable solution. On the other hand he may still say that his task is to find the entire range of theories, leaving the reader to complete his own unification.

Dealing with the herd instinct, the author criticizes the generally accepted McDougall hypothesis, comments on the works of other authors and summarizes his own opinions.

> We have so vacillated from side to side, picking up one theory and then dropping it for another, considering this and that view only to point at its insecurity, embarking upon a promising trail without the necessary time to follow it up, that we are hard put to enunciate any but vague and tentative conclusions. We might, however, advance the view that a herd-instinct may perhaps exist as an innate tendency towards gregariousness, but that it has become so modified in man, and obscured in its real effects by the growth of intelligence, that it has become a factor of diminishing importance.

Those who are interested in sociology will find utility in the references on crime, delinquency and amentia, law and its administration, education, sociological problems—war, social unrest, culture, prostitution, morals and mental health, analysis of myths and religions *et cetera*.

The references are so numerous that a full description is beyond the scope of a review.

Enough has been written to assure any reader who needs a reference work on the mechanisms underlying problems in behaviour that "Psychopathology" is worthy of a place on his shelves.

PROGRESS IN PATHOLOGY.

THE object of the "Recent Advances" series is to present to the non-specialist new trends of thought and new work that has not as yet been absorbed into the standard textbooks. The fifth edition of Hadfield and Garrod's "Recent Advances in Pathology" must therefore receive a certain amount of adverse criticism.[1] The shortage of paper alone should have been a perfectly good reason for omitting those chapters which are much the same as in previous editions and which in some instances are well treated in standard textbooks. The chapters dealing with the endocrine glands, cardio-vascular, respiratory and digestive systems could perhaps have been omitted. This would have allowed the sketchy chapter on the reticuloses and reticulosarcoma to be adequately expanded into a more coherent account.

Those who acquire this new edition will probably do so on account of the excellent chapters on liver disease and Bright's disease. The pathology of infective hepatitis and homologous serum jaundice and the effects upon the liver of protein deficiency are well presented. Ellis's clinical classification of nephritis is adequately illustrated, mainly by his own photomicrographs, and should satisfy those who seek for a relatively simple working classification of Bright's disease.

PROGRESS IN PUBLIC HEALTH.

IN "Recent Advances in Public Health", the Medical Officer of Health and School Medical Officer to the City of Salford, England, Dr. J. L. Burn, has produced a book which should act as a source of inspiration and encouragement to all workers in the sphere of public health administration.[2]

It reveals in its 37 chapters how the work of the public health expert has permeated all walks of life, and that the provision of pure water and sewerage is only a very small portion of his requirements to build up a healthy community.

The book is so far-reaching and so interesting to read that it could be read by members of parliament and of municipal and shire councils in Australia with considerable advantage to the state of the public health. It is divided into three main divisions: (*a*) "Public Health and the Individual." (*b*) "Public Health and the Community." (*c*) "Public Health and the Environment."

It illustrates in no small measure the purposes of the Oxford Institution of Social Medicine: (i) To investigate the influence of social, genetic, environmental and domestic factors on the incidence of disease. (ii) To seek and promote measures, other than those usually employed in the practice of remedial medicine, for the protection of the individual and of the community against such forces as interfere with the full development and maintenance of man's mental and physical capacity.

[1] "Recent Advances in Pathology", by Geoffrey Hadfield, M.D., F.R.C.P. (London), and Lawrence P. Garrod, M.A., M.D., B.Ch. (Camb.), F.R.C.P. (London); Fifth Edition; 1947. London: J. and A. Churchill, Limited. 8″ × 5¼″, pp. 372, with many illustrations. Price: 21s.

[2] "Recent Advances in Public Health", by J. L. Burn, M.D., D.Hy., D.P.H.; 1947. London: J. and A. Churchill, Limited. 8¼″ × 5¼″, pp. 418, with many illustrations. Price: 25s.

"MORPHOLOGIC HÆMATOLOGY."

ACCORDING to William Dameshek, hæmatology began as morphology; it is therefore appropriate that the first special issue of *Blood* should be entitled "Morphologic Hæmatology". The cells of the blood were recognized and studied in the very early days of microscopy, but no real progress was made until the time of Ehrlich, who transformed the study of the blood cells by the introduction of the brilliant aniline stains now in use. The discovery of the treatment of pernicious anæmia by liver and liver extracts brought a dynamic interest into hæmatology, and the increasing use of bone marrow smears and biopsies added variety and importance. Attempts have been made to correlate the staining of blood cells with microchemical investigations, and Dameshek states that the science of "histochemistry" is bound to progress. Newer morphological methods involving phase microscopy, electron microscopy, ultra-violet absorption techniques, fluorescence microscopy, and micro-incineration are already available as methods to open up new vistas in the field of hæmatology. Marrow culture methods offer great promise, and two articles on this subject by Plum are included in this book. Dameshek's preface and an introduction by Oliver P. Jones are followed by eighteen articles which record original work on the cells of the blood and bone marrow in health and disease, in man or in animals. Some of these, such as "Normal Bone-Marrow as Obtained by Sternal Puncture", by Stewart L. Vaughan and Frances Brocksmyre, are of general interest; others, such as "A Physiological Study of Erythroblasts in the Duck" and "Certain Characteristics of the Leukocytes of Guinea-Pig Blood, with Particular Reference to the Kurloff Body", are probably of interest only to research students.

No pains have been spared to make this volume a fine material achievement. The title page sets out an imposing list of editors, including contributory editors from Europe and Latin-America. The articles are technically of a very high standard, fully documented, and illustrated when necessary by excellent photomicrographs. The paper, type and general production could hardly be bettered. However, the book will be judged on the quality of the contributions included in it and not solely on the way in which they are presented.

DORLAND'S MEDICAL DICTIONARY.

THE twenty-first edition of Dorland's well-known "American Illustrated Medical Dictionary" has been published.[2] It covers the terms used in medicine, surgery, dentistry, pharmacy, chemistry, nursing, veterinary science, biology, medical biography and so on. There are in its pages no less than 880 illustrations, including 233 portraits. The wisdom of the inclusion of illustrations, particularly portraits, in such a volume has been questioned, but they do add a certain interest to the work. A great many of the diagrams are indispensable.

The type in which the pages are set is clear; the words to be explained appear in heavy type and this is an aid to quick reference. Greek derivations are set in Greek characters. The explanations to words are not skimped; and in this way the work is saved from being unduly dull. With the matter itself we can find no fault—we have searched in vain for omissions. The abbreviation Ch. for *chirurgia*, surgery, does not appear. We have always thought it a pity that this is omitted from some medical dictionaries; the result is that medical graduates are often described in newspapers as Masters of Chemistry. This dictionary may be recommended with every confidence.

[1] "Morphologic Hematology", editor-in-chief, William Dameshek, M.D.; Special Issue No. 1 of *Blood, The Journal of Hematology*; 1947. New York: Grune and Stratton. 10″ × 7″, pp. 208, with illustrations. Price: $4.75.

[2] "The American Illustrated Medical Dictionary", by W. A. Newman Dorland, A.M., M.D., F.A.C.S., with the collaboration of E. C. L. Miller, M.D.; Twenty-First Edition; 1947. Philadelphia and London: W. B. Saunders Company; Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9¼″ × 6¼″, pp. 1660, with many illustrations, some of them coloured. Price: 59s. 6d.

The Medical Journal of Australia

SATURDAY, APRIL 10, 1948.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE LUNACY ACT OF NEW SOUTH WALES.

In New South Wales the *Lunacy Act*, 1898, has been amended on several occasions. The composite act, which comprises the most recent amendments of 1946, is known as the *Lunacy Act*, 1898-1946. Since in the course of their practice medical men and women have from time to time to carry out certain duties provided for in this act, it is necessary that they should be conversant with its provisions. A year or two ago certain happenings in the courts of law directed the attention of the New South Wales Branch of the British Medical Association to recently introduced provisions of the act, more particularly as they affected the certifying medical practitioner. Careful scrutiny of the act has shown that the medical practitioner must take certain precautions for his own protection.

The act as it stands today has evolved from the time when there was no provision for the treatment of persons who might voluntarily seek treatment at mental hospitals. In 1934 the act was amended in such a way that provision was made "for the reception of voluntary patients into hospitals for the insane and licensed houses and for their care and maintenance therein". It was also planned to facilitate admissions to reception houses. According to the act "the Governor may, by notification in the Gazette, appoint such houses and premises as he may think expedient for the reception and temporary treatment of the insane, and every such house and premises shall be a reception house for the insane. . . ." According to the original act a person could be received into a mental hospital upon a request in writing together with a statement setting out certain particulars and two medical certificates signed by two practitioners who had examined the patient and signed the certificates independently of one another. In 1934 the following subsection was added:

A person may be received into and detained in a reception house upon the certificate of one medical practitioner in the form of Schedule 2A; a person may also be received into and detained in a reception house on his own written request or on the written request of a relative or friend, if the medical officer of the reception house certifies at the foot of such written request that in his opinion the person proposed for admission is a suitable case for admission to the reception house for observation and treatment.

Schedule 2A reads as follows:

I, the undersigned medical practitioner, hereby certify that on the day of , 19 , I personally examined [*name of person in full*], and am of the opinion that he is a suitable case for admission to the [*name of institution*] for observation and treatment.

Dated this day of , one thousand nine hundred and .

[Signature.]
[Place of abode.]

Two provisions in the act regarding proceedings by which persons of unsound mind may be placed under restraint should be noted. The first is that when any person is admitted to a reception house under the subsection dealing with committal on a certificate in the form of Schedule 2A, the fact of his admission shall as soon as practicable be notified to a police constable by the medical officer or officer in charge of the reception house, and that constable or any other constable may without any order apprehend and take such person before two justices to be dealt with under another section (Section 6) of the act as if such person were a person deemed to be insane and found by the constable wandering at large. The second provision to be noted is that if any medical practitioner grants a certificate in the form of Schedule 2A of the act without having seen and personally examined the person to whom it relates, at the time specified in such certificate, for the purpose of ascertaining the condition of such person to the best of his knowledge and power, he shall for every such offence be liable to a penalty not exceeding fifty pounds.

The New South Wales Branch Council submitted to Counsel for an opinion the two following questions:

1. Would a medical practitioner be open to any liability or claim or action for damages or otherwise if he took steps forcibly to remove a person to a reception house in respect of whom a certificate under this sub-section had issued, or assisted in the forcible removal thereto?
2. Would a medical practitioner be liable to any action for damages for defamation or otherwise if he should issue a certificate under this sub-section without the consent of the person to whom such certificate refers to a third person?

Before he answers the questions, Counsel quotes Section 172 of the *Lunacy Act*, which is as follows:

(1) No suit or action shall lie against any person for or on account of any act, matter, or thing done or commanded to be done by him, and purporting to be done for the purpose of carrying out the provisions of this Act, if that person has acted in good faith and with reasonable care.

(2) No such suit or action as aforesaid shall be commenced but within three months after the alleged cause of action, or, in the case of a suit or action by a person who has been an insane person or patient, but within three months next after the making of a superseding order, or next after the discharge of the patient.

(3) Proceedings in such suit or action as aforesaid may, on summary application to the Court, be stayed upon such terms as to costs or otherwise as the Court may think fit, if the Court is satisfied that there is no reasonable ground for alleging want of good faith or reasonable care, or that the said proceedings have been commenced after the expiration of the three months aforesaid.

Having mentioned two decisions in which Section 172 was considered, Counsel concludes from them that any action at law brought against a medical practitioner (who has given a certificate in the form of Schedule 2A) for any act done or purporting to have been done for the purpose of carrying out the provisions of the act must be brought within three months after the doing of the act complained of (or within three months after discharge in the case of an insane person or patient), and then such action may proceed to trial only if the Court is satisfied

that there is reasonable ground for the plaintiff alleging want of good faith or reasonable care. This statutory protection, Counsel points out, depends upon the fact that the act complained of was done or purported to have been done for the purpose of carrying out the provisions of the act. Counsel discusses the provision for the voluntary admission into reception houses of persons suffering from mental disorders, and expresses the view that a medical practitioner who may give a certificate in the form of Schedule 2A for the purpose of Section 4(2) is justified only in issuing it to the patient if he is willing to act on it, or, if not, then to some person who is in such a position of relationship or friendship with the subject of the certificate as would enable that person to persuade him voluntarily to enter a reception house. Counsel therefore answered the first question put to him in the affirmative. "The Act does not authorise a doctor forcibly to remove a person, after issuing a certificate in form 2A, to the Reception House or to assist in his forcible removal thereto. Such an act, if done, would not be an act done or purporting to be done for the purpose of carrying out the provisions of the Act, i.e. sec. 4(2); and section 172 would afford no protection whatsoever to a defendant in an action for assault or false imprisonment."

Counsel's answer to the second question is just as important to the practitioner as his answer to the first. He states that it seems clear that it is libellous to write and publish of a man that he is insane or that he is not quite responsible for his actions. To issue such a certificate to a third person, without the consent of the subject of it, is actionable. "If such publication be an act done or purporting to be done for the purpose of carrying out the provisions of the Act, which would primarily be a question of fact (i.e. was it done to facilitate the voluntary admission of the patient who was in need of treatment for mental disorder to a Reception House?), the action would be incompetent after the period mentioned in Section 172 and it would be stayed if brought within the period should the Court be satisfied that the medical practitioner issued the certificate, and issued it to such third person in good faith and with reasonable care." Counsel fails to see what other form of action would be open to the subject of a certificate in form of Schedule 2A except an action for negligence, "if the person was in fact not a suitable case for admission to a reception house".

It is clear that the course of action to be taken by a medical practitioner is beset with difficulties. What he has to do may be summed up by the statement that, having made a careful examination of the patient, and having determined that observation in a reception house is necessary, he should write a certificate in the form of Schedule 2A, and give it, enclosed in a sealed envelope, to the patient or to a responsible relative for transmission to the officer in charge of the reception house. The conclusion of the whole matter is that some amendment should be made to the act to safeguard the actions of a medical practitioner. It should be possible to do this and at the same time to secure the rights of the patient and his safety from unnecessary admission to a reception house. The whole matter would be much simpler if people could be made to look on a mental upset as an event comparable to an upset of the musculature, the heart or the alimentary tract, and as free from stigma as any of these.

Current Comment.

THE ADMINISTRATION OF PENICILLIN BY MOUTH.

THE best methods for the administration of penicillin are now well worked out and the accepted routes also. It may be somewhat academic to inquire what is the value, if any, of such a wasteful route as the upper part of the digestive tract and the simple method of swallowing; however, interesting and comprehensive work has recently been carried out by H. C. Stewart and J. R. May, which gives some exact information.[1] The method of estimation of penicillin blood levels used was the improved technique of Fleming and Smith, and all factors thought relevant were examined with the blood level as a criterion. No attempt was made to treat patients suffering from infections. The authors point out that in some of the previous work on the subject very large doses of penicillin were administered to patients infected by very sensitive organisms. In their own work they used exclusively healthy adults, men between twenty and forty years of age. Duodenal intubation was used in a few experiments, but as a rule the penicillin was administered in about four ounces of water, a quantity which prevented the unpleasant taste from being too noticeable. It was found that the absorption of penicillin was practically always better when the stomach was empty. The curve of the blood-penicillin levels rose more slowly after oral administration, of course, and did not assume such a height as after intramuscular injection. An average of sixteen experiments showed that the blood levels after oral and intramuscular administration indicated that the two routes were comparable during the period from about three-quarters of an hour and one and a half hours after the dose, but not at the beginning or at the end of the test. The effect of gastric acidity was measured by comparison of the antibiotic value of penicillin after it had been mixed with gastric juices of different composition. This factor became significant only when the pH of the gastric juice was less than 3·0. There was no evidence that the type of penicillin made any difference in its absorption from the upper portion of the digestive tract. The I, II, III and K varieties were tested, but no significant differences were found. In order to make sure that the particular samples tested were intrinsically capable of being freely absorbed, the penicillin used for these experiments was extracted from urine after previous administration; each specimen tested had thus previously been proved capable of absorption. In view of the belief that the secretions of the stomach were destructive to penicillin, capsules had been advised by other workers. Stewart and May's work, having demonstrated that gastric secretion had little such influence, suggested that capsules of any kind were unnecessary. This was proved by the use of capsules made in such a way that they would dissolve at different points in their journey down the alimentary tract; in fact it was found that absorption diminished steadily at the lower levels. The best absorptive area for penicillin, as for many other substances, appeared to be the upper part of the tract. As it has been found that there seems to be some advantage in giving penicillin in solution with glucose, the effect of the addition of glucose to the oral dose was tried. There appeared to be some improvement in the absorption rate, but chiefly in those persons who are naturally good absorbers. Glucose did not improve the capacity of a poor absorber.

One of the interesting features of this work is the finding of perceptible variation of absorption in individuals. The great impetus given to biochemical assays in modern therapeutic methods has shown how common and important is the occurrence of this individual variation. It was to be expected that variation would be found in the absorption of penicillin by mouth, and if this route is to be used for any reason a suspected lower capacity for ready absorption would need to be countered

[1] *The Lancet*, December 13, 1947.

by larger dosage. One further observation of interest should be mentioned—the failure to demonstrate any significant production of penicillinase in the intestine. A limited number of tests were made of organisms obtained by duodenal intubation, but the conclusion was reached that any destructive effect from this cause was negligible. Stewart and May think that in order to ensure an effective blood level it would be advisable to give by mouth ten times the dose judged appropriate by intramuscular injection. They finally stress the importance of the unexplained factor of individual absorption from the duodenum and intestine. This they believe is probably the most important factor of all; it cannot be foretold, and it can be determined only by estimations of the penicillin level in the blood.

THE MEULENGRACHT TREATMENT OF HÆMATEMESIS.

WHEN E. Meulengracht introduced his "free feeding" method of treatment of bleeding ulcer it was received with general caution. In 1935 he published[1] his first paper in an English journal, describing the results of the treatment in 251 cases of hæmatemesis and melena believed to be due to genuine ulcer hæmorrhage, and H. L. Tidy, in "The Medical Annual, 1937", drew attention to this paper with approval. Since then the method, which consists essentially of giving the patient a liberal "purée diet", with alkalis, from the day after admission to hospital, has found its way into standard textbooks even though it may not have been universally adopted. Meulengracht himself has continued to use the method and now, with the ending of Denmark's wartime isolation, he has reported[2] his results from the treatment of 1031 patients between 1931 and 1946. These were all patients with gross hæmorrhage, indicated by distinct hæmatemesis or directly visible melena, who were treated at Bispebjerg Hospital at Copenhagen; Meulengracht employed his standard method of treatment as a routine, so that there was apparently no form of selection of patients apart from the elimination of those with small quantities of blood in the vomitus or with only chemically detectable melena. Of the 1031 patients, 1005 were discharged from hospital after completion of treatment, and 26 died while in hospital, a mortality rate of 2·5%. An analysis of the fatalities is interesting. All but one of the patients who died were over the age of forty years, and half of the number were over the age of sixty years, although the majority of the 1031 patients treated belonged to the lower age groups. In six cases death was entirely or in the main due to causes other than bleeding, and in five death occurred within twenty-four hours of admission (that is, before the "free feeding" commenced), so that there were actually only 15 deaths associated with the treatment. This would make the mortality rate 1·5%, which compares more than favourably with the results from other forms of treatment. In most cases in which bleeding was considered to be the immediate cause of death large eroded blood vessels were found *post mortem*. Gastric ulcers were in higher proportion amongst the patients who died than amongst the general body of those treated; they apparently have a greater tendency to cause fatal hæmorrhage.

Meulengracht, having made his case for the value of the treatment in ensuring a high survival rate, then asks the frank question whether the treatment of those who died had not only been useless but had even done harm. He points out that five patients died shortly after admission to hospital and could neither eat nor drink; eight died in the course of two to five days and were too ill to eat or drink much; even those who died in five or ten days took little fluid or nourishment. In his view it was not the treatment that did harm, but the lack of it; these patients, in a still greater measure than those with less severe illness, needed all the support which they could get. He considers that, seen in retrospect, a few of the patients might have derived benefit from surgical treatment, but their selection during life would have presented considerable difficulties. There is an increased tendency to operate on these patients nowadays, as was pointed out in these columns on January 18, 1947; but, to judge from the information given as to age, general condition and pathological state found *post mortem*, it does not seem likely that surgery would have saved many in this series. Meulengracht admits quite frankly, however, that he employed blood transfusions on far too small a scale, and feels that his results can be improved by the use of transfusions and similar measures. Perhaps, too, these measures would bring more of the patients within the ambit of the surgeon. However, Meulengracht seems to have justified his method by results, at any rate as compared with other medical régimes. The points in its favour are fairly obvious, and even though, as Christian points out in a recent edition of "Osler", the general experience is that most patients while active bleeding is taking place decline to eat freely, this does not lessen the value of the system when it can be applied.

[1] *The Lancet*, November 30, 1938.
[2] *Archives of Internal Medicine*, December, 1947.

RAYNAUD'S DISEASE AND SYMPATHECTOMY.

THE effects, clinical and physiological, of sympathectomy of the upper limb have been the subject of much controversy, as readers of this journal will remember. From the practical angle the value or otherwise of sympathectomy in the treatment of Raynaud's disease and allied vascular disorders is a matter of some importance, but the procedure has had a fluctuating popularity. On July 15, 1944, we referred in these columns to the waning enthusiasm for operations on the sympathetic nervous system in the treatment of vascular disorders, and discussed the view put forward by Mufson that Raynaud's disease had a psychosomatic basis, emotional forces initiating abnormal sympathetic impulses which caused angiospasm and exposure to cold acting as a local aggravating factor. This may quite well be so, but it does not rule out sympathectomy, although the procedure may be regarded as merely symptomatic treatment, and a recent report contains some interesting clinical results. H. Barcroft and G. T. C. Hamilton[1] have followed up the results of preganglionic section in 52 cases of Raynaud's phenomenon and recorded the clinical and physiological effects. Only one to six months had elapsed since operation on 16 limbs of which the hands were affected, but in all cases there was decided clinical improvement so far; in 14 cases no further attacks had occurred, and in two cases the attacks were less frequent and less severe; all the patients considered the operation worth while. The results in the other 36 limbs were followed up for periods of one to six years; in 18 cases there was no recurrence, in 14 cases the attacks were much less distressing, and in four cases there was no improvement; in all cases but the last four the patients considered the operation worth while. Physiological investigation of the limbs showed the complete absence of all vasomotor and sudomotor reflexes for several months after operation in all cases, indicating, according to Barcroft and Hamilton, that the operation had completely severed sympathetic nervous connexion between the brain and the hand. In some cases vasomotor and sudomotor reflexes later returned, most likely, according to these workers, owing to the regeneration of sympathetic nerve fibres. The new nerve path appeared, however, to be inferior functionally to the original, as the vasospasm did not recur in most cases. Recurrence of symptoms took place in less than one month in one-third of the cases in which it occurred and in less than six months in four-fifths of the cases. At least in the first of these groups it was presumably due to a "local fault" in the blood vessels of the hand, as reflex sympathetic activity was still absent. Although these results are difficult of interpretation, it seems wrong to deny that the sympathectomy was of very real benefit and must still be considered in the management of what can be a most distressing condition.

[1] *The Lancet*, March 20, 1948.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Removal of the Wrong Eye.

H. M. TRAQUAIR (*British Journal of Ophthalmology*, January, 1947) discusses the subject of "removal of the wrong eye" and is struck by the almost complete absence of mention of the subject in ophthalmic and medico-legal literature. He regards the current stories (of which one concerns a well-known surgeon who removed the wrong eye and then rushed into an adjoining room and shot himself) not as evidence of the disaster, but merely as pointing out that where there is smoke there is fire. References in the literature contain warnings against the risk of the accident and advice as to how it may be avoided. For the removal of a wrong eye two postulates are essential: the patient must be under a general anæsthetic, and the eye to be removed must not be obviously different in appearance from the other. Secondary or adjuvant causes include omission to indicate the eye by a mark on the forehead or even delegation of the marking to a nurse or house surgeon, an error in the notes, or omission to verify the eye to be removed by examination or reference to notes immediately before the operation. The diseases concerned in actual instances have been intraocular tumour, glaucoma and sympathetic ophthalmia. In every known case a general anæsthetic was used. In infants and children this risk must be taken and it is the duty of the surgeon personally to take proper precautions. If a general anæsthetic is to be given to either child or adult, administration should not be commenced until the surgeon is present. The only infallible preventive, if any measure can be infallible, is the use of local analgesia. A paragraph on this subject should be included in every textbook in which removal of the eye is mentioned.

Post-Operative Complications of Cataract Extraction.

WILLIAM F. HUGHES AND WILLIAM COUNCILMAN OWENS (*Archives of Ophthalmology*, November, 1947) review complications which occurred in the course of 2086 consecutive cataract extractions. Incomplete closure of the wound is in their opinion almost completely prevented by the use of silk corneo-scleral sutures. However, the complication is more likely to occur if there has been vitreous loss. They condemn the use of absorbable sutures. Prolapse of iris occurred in 56 cases and in 43% of cases the prolapse occurred after the eleventh post-operative day. The chief cause was incomplete closure of the corneal wound. With corneo-scleral sutures the incidence of iris prolapse was the same after round pupil extractions with iridotomy as after extractions combined with full iridectomy. Delayed reformation of the anterior chamber and late collapse of the anterior chamber were always associated with filtration of aqueous through the corneal incision. Air was injected into the anterior chamber in some cases in which the chamber was collapsed for seven to ten days. Persistent haziness of the cornea was sufficient to reduce final vision to below $^{20}/_{30}$ in eleven cases. It may be due to excessive instrumentation at the time of operation, trauma in placement of sutures, post-operative irido-cyclitis and poor wound closure. Hæmorrhage into the anterior chamber occurred in 195 cases. In addition hæmorrhage followed the removal of corneo-scleral sutures in 3·6% of 1030 cases in which they were used. Examination of their three cases of expulsive hæmorrhage revealed no correlation between systemic hypertension and expulsive chorioidal hæmorrhage, and the authors state that attempts to reduce blood pressure pre-operatively are not indicated. There appeared to be three main causes of post-operative irido-cyclitis, namely, retained lens matter, rupture of the hyaloid membrane of the vitreous and low-grade infection. In dealing with irido-cyclitis due to retained lens matter they recommend desensitization by Burkey and Henton's technique. Secondary glaucoma occurred in 87 cases and was most often preceded by iridocyclitis. Operation was performed in 65 cases. Where the angle is blocked by inflammatory debris or anterior synechiæ cyclodialysis is the operation of choice. In a few cases trephining was carried out, but this should be reserved for eyes with a deep anterior chamber. An intractable secondary glaucoma after cataract extraction may be caused by a down-growth of epithelium into the anterior chamber. Retinal detachment occurred in 31 cases, the incidence of this complication rising with increased amounts of vitreous loss. Purulent endophthalmitis occurred in 21 cases.

Tenotomy of the Superior Oblique Muscle for Hypertropia.

R. N. BERKE (*Archives of Ophthalmology*, November, 1947) discusses the treatment of hypertropia associated with overaction of the superior oblique muscle. He reviews literature, gives indications for tenotomy of the superior oblique muscle, describes the anatomy of the muscle and the operative technique, and finally presents case reports. He states that today most ophthalmic surgeons are agreed that tenotomy of the superior oblique muscle is out of favour and comments that tenotomy of the inferior oblique muscle was similarly regarded thirty or forty years ago.

"Dicumarol" and Rutin in Retinal Vascular Disorders.

ANGUS L. MACLEAN AND CHARLES E. BRAMBEL (*American Journal of Ophthalmology*, September, 1947) present their findings in twenty-one cases of vascular retinopathies treated with "Dicumarol" and rutin. The four processes involved in the vascular retinopathies are hæmorrhage, thrombosis, atherosclerosis and exudative congestion, and these are considered under three headings: (*a*) thrombosis primary and hæmorrhage secondary, (*b*) hæmorrhage primary and thrombosis secondary, (*c*) degenerative retinopathy. In the first category are the clinical conditions of tributary occlusion and central vein occlusion. In these cases "Dicumarol" or other in-vivo anti-coagulants are indicated. Also rutin or other substances similar to vitamin *P* would be indicated to improve capillary integrity. When hæmorrhage is primary two conditions to be considered are hypertension and idiopathic capillary weakness. Under these circumstances rutin or other substances of the vitamin *P* type would be indicated to improve capillary integrity. They state that "Dicumarol" cautiously administered would be indicated to inhibit the thrombotic process, and the routine concomitant administration of these two drugs should increase the rate of absorption of the hæmorrhages and the possibility that new ones will be reduced. In Eales's disease the same therapeutic indications apply. In degenerative retinopathy there is impaired vascular efficiency resulting in localizing degenerative and proliferative processes with exudative congestion. Administration of "Dicumarol" should facilitate circulation and rutin would improve capillary integrity. No patient should be given "Dicumarol" unless laboratory facilities are available to check the prothrombin clotting time. An initial determination of prothrombin clotting time was made on each patient before "Dicumarol" was given. The first dose was 300 milligrammes given orally and the next test was made forty-eight hours later. A series of subsequent determinations were made at two-day intervals with dosages of 100 to 300 milligrammes to maintain a coagulation activity level of 50% of normal. After it was found that the response could be fairly well predicted the patient was continued on "Dicumarol", returning once per week for prothrombin clotting time determinations and succeeding doses. Concomitant oral administration of rutin in doses of 60 milligrammes daily was the usual routine and was kept up for the duration of the combined therapy. The authors conclude with a detailed report on six patients treated.

Posterior Sclerotomy for Subchorioidal Hæmorrhage.

PETER A. DUEHR AND CLIFFORD D. HOGENSON (*Archives of Ophthalmology*, September, 1947) report in detail a case of subchorioidal hæmorrhage treated by posterior sclerotomy. The patient, a man, aged fifty-four years, had had a successful intracapsular cataract extraction in the right eye. Six months later extraction of the left lens was attempted. The extraction was extracapsular, and during the tying of the corneo-scleral and conjunctival sutures the eye became hard and the patient complained of acute pain in the eye. There was perception of light in the far temporal field only. A Graefe knife was thrust through the globe in the inferior temporal quadrant twelve millimetres from the limbus and a large amount of bright blood escaped. The process of reinserting the knife was repeated at least six times and the amount of blood that drained from the eye was estimated at thirty millilitres. Six months later the vision in the left eye was $^{20}/_{100}$ with correction. The authors conclude that posterior sclerotomy should be tried in instances of expulsive hæmorrhage.

Solutions Used with Contact Lenses.

THEODORE OBRIG (*Archives of Ophthalmology*, November, 1947) conducted a series of experiments in an endeavour to find out causes and means of prevention of corneal clouding by solutions used with contact lenses. Investigating

the effect of an accumulation of carbon dioxide, the author concluded that the contact lens could be worn as long with solutions saturated with carbon dioxide as with the same solution without the carbon dioxide before corneal clouding took place. On the basis that clouding is due to isolation of the cornea from atmospheric oxygen, a series of solutions to be used were first saturated with oxygen. The author concluded that the presence of oxygen was soothing and in some cases lengthened the wearing time before corneal clouding took place. Experiments on the effect of variation of osmotic pressure indicated that osmotic pressure was an important factor in a solution for use with contact lenses, and further the useful wearing time of contact lenses could be lengthened by the use of three successively stronger solutions of the more usual type. The addition of amino acid was found to lengthen the wearing time of contact lenses; the preparation used was "Parenamine", a 15% solution of amino acids. The addition of methyl cellulose increased the wearing time with a "Parenamine" and potassium carbonate solution.

Absorbable Corneo-Scleral Sutures in Cataract Surgery.

L. J. ALGAR (*Archives of Ophthalmology*, November, 1947) is of the opinion that in cataract surgery the corneo-scleral suture should be an absorbable one. He bases his conclusion on experience in 76 cases in which he used plain 0000 atraumatic surgical gut. His method of suture is the Stallard suture combined with a Van Lint flap. The extraction is combined with a marginal iridectomy at the eleven and one o'clock positions, and at the end of operation a miotic is instilled. He claims that the lessened feeling of foreign body in the eye produces lessened squeezing and blinking which are conducive to post-operative hæmorrhage and iris prolapse. Finally the method eliminates the need for removal of sutures, a procedure which may cause rupture of the wound.

OTO-RHINO-LARYNGOLOGY.

Malignant Melanoma of the Nasal Mucosa.

CHARLES C. GRACE (*Archives of Otolaryngology*, August, 1947) states that, whereas the malignant melanoma of the skin frequently commences in a nævus, that arising in the eye is not preceded by a benign lesion. Similarly on the feet and genitalia where nævi are rarely present, melanomata arise apparently not from moles. It would appear that melanoma of the nasal mucosa does not arise from a nævus, for the presence of this benign lesion in the nasal fossa has never been confirmed. Pigment is lacking in the lower portion of the nasal fossa; it is only at the level of the upper olfactory portion that the presence of pigment can be established. The disease is rare and of interest because melanomata usually develop in areas where the tissues normally contain pigment. The incidence is approximately the same for the two sexes and the disease is usually observed in persons of middle age. While there is still some uncertainty as to the exact cellular origin of melanomata, evidence has been proffered of their origin from basal epithelium, from fibroblasts, from the end apparatus of cutaneous sensory nerves, or from specialized mesodermal cells, the melanoblasts or chromatophores, the last-mentioned being regarded as a specific cell controlling the production and transport of pigment. The microscopic picture is highly variable; it may exhibit carcinomatous or sarcomatous structure or it may simulate an endothelioma or even a lymphosarcoma. In the nose, in spite of the fact that pigment may be found in the mucosa of the upper portion and is absent in the lower portion, melanomata arise in that portion which is without pigment, either on the septum or on the lateral wall. They are stated never to arise in the superior portion of the nasal mucous membrane. Some authors have suggested that melanoma of the nose may be induced by repeated removal of nasal polypi or other trauma. There was a history of removal of polypi in 18 of 48 case histories studied. Unilateral nasal obstruction and repeated epistaxis are the usual early symptoms. The discharge of an inky-black serous fluid is frequently present. The lesion may remain quite small and its importance may not be from any local symptoms but rather in the widespread metastasis. The melanoma is variously described as a dusky-purple, reddish-grey, reddish-black or black growth, a cauliflower mass bleeding readily on the slightest manipulation, and a tumour resembling a ripe mulberry. Occasionally the lesion may grow until nasal deformity is produced and a mass may protrude from the naris. Histological study is essential and it may be necessary to establish the presence of true melanoblasts by demonstration of the presence of the oxidase ferment capable of transforming the colourless chromogenic material of the blood into melanin. Radiotherapy seems to be generally unavailing. The slow growth of the primary tumour as compared with the rapid dissemination of metastatic lesions is an important consideration in planning treatment. Radical removal including a wide margin of normal tissue would appear to offer a reasonable chance of cure. Deformity may thus result, but it should nevertheless be undertaken even though the lesion is small. The prognosis is usually grave. In some instances the tumour remains localized for a long period, and it may be possible successfully to remove the primary lesion and any involved cervical glands and intervening lymphatics. The average survival period is two to three years from the onset of the primary lesion. Death usually ensues from metastatic involvement of the liver or other vital parts. The case reported is apparently the first one to be recorded in the literature of a melanoma occurring in a Negro.

Œsophageal Perforations.

F. L. LEDERER, A. A. GROSSMAN AND W. A. DONNELLY (*Annals of Otology, Rhinology and Laryngology*, December, 1947) state that there are two schools of thought in the treatment of œsophageal perforations: the interventionists who urge early cervical mediastinotomy, and the conservative group who would rather wait for complications to occur before they advise surgery, if they would advise it at all. The antibiotics are important if their limitations are understood. Penicillin is especially useful during the immediate period of watchful waiting following the injury, but has not obviated the necessity of surgical intervention, especially when complications such as mediastinitis, pleural effusion or empyema have occurred. Pearse in 1938 in a series of 64 cases of œsophageal tears reported a mortality rate of 27% in spite of early cervical mediastinotomy in the pre-penicillin era. Among patients treated by watchful waiting alone, there was an 87% mortality. Other reports showed similar results in the two groups. In the past the surgeon has often performed gastrostomy to rest the œsophagus while awaiting the possible development of secondary infective complications. Penicillin has supported the non-interventionists. The following course is recommended when a diagnosis of œsophageal perforation is suspected. (i) One hundred thousand units of penicillin are given every two hours. (ii) Nothing is given by mouth. Intravenous therapy may be instituted for feeding purposes. Gastrostomy or Levine feeding tubes may be necessary. (iii) The patient is placed in the Trendelenburg position to prevent secretions trickling down to the involved area. (iv) Oxygen (100%) is administered continuously by mask. (v) Sedation may be used every four hours if necessary, but care should be taken not to depress the respiratory centre. (vi) Bacterial cultures, both anaerobic and aerobic, should be prepared and polyvalent gas-gangrene antiserum and tetanus antitoxin should be administered. (vii) Small and repeated blood transfusions are of value. (viii) Sulphonamides and streptomycin should also be administered in appropriate fashion. Surgery may still become necessary. In all cases of high œsophageal perforation, early cervicotomy is advocated. The other measures as outlined should be employed simultaneously. In other cases certain definite indicators are to be watched for which will call for intervention. These are: (i) X-ray evidence of air in the tissues or of progressive changes in the thorax such as advancing effusions; (ii) clinical signs and symptoms of prevertebral or mediastinal emphysema. (iii) changes in the white blood cell count, the pulse rate and the temperature. X-ray examination should be made of the neck and chest and be repeated daily or more often, and blood counts should be frequently made. Should there be evidence either clinically or radiographically that infection is spreading, immediate surgery should be carried out in the area indicated. A cervical mediastinotomy may suffice, or posterior mediastinotomy may be needed if there is evidence of an increase in volume of pleural effusion. Amongst the most common symptoms of œsophageal perforation are pain, often located at the point of perforation, but not infrequently localized between the shoulder blades, dysphagia, sometimes associated with expectoration of blood, and dyspnœa, frequently associated with extreme restlessness. Three cases are discussed, illustrating the application of the indicators as outlined and the response to treatment.

British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at Wangaratta on October 25, 1947, the President, DR. A. E. COATES, in the chair. The meeting took the form of a series of clinical demonstrations by members of the staff of the Wangaratta District and Base Hospital, followed by a paper read by DR. A. M. HILL. Part of this report appeared in the issue of April 3, 1948.

Pelvic Cellulitis.

DR. D. D. BROWNE showed a young married woman who had had recurrent febrile attacks of uncertain origin since August, 1946. She was the mother of two children, aged two and a half years and one year and two months respectively. The second confinement was apparently normal and the baby was healthy, but on the eighth day of the puerperal period there had been a sudden copious discharge from the vagina as if an abscess had burst. The temperature rose to 102·6° F. and the pulse rate increased to 130 beats per minute. A week later she was having sulphadiazine therapy for pyelitis. Though for five weeks the charts were strongly suggestive of the presence of septicæmia and a thorough investigation was carried out, no cultures were grown and no conclusive diagnosis was made. Two months afterwards she was febrile again with pains and aches in muscles and joints. She had had many similar attacks. For four months from January, 1947, she had received a lot of treatment in the western district of Victoria and had not been well at any time. Dr. Browne had seen her first in August, 1947, and had elicited pain on the slightest movement of the cervix by digital examination. A negative result had been reported on a blood specimen submitted for the gonococcal complement-fixation test. She also had pain about the left hip and the right elbow, and left-sided adductor spasm was present. A week afterwards the trouble in the left hip was worse and a skiagram was prepared; the appearances in this were regarded as within the limits of normality. Dr. Browne concluded by summarizing the position. The woman had had twelve or fourteen attacks in fourteen months, the features of which were feverishness and aches and pains in muscles and joints. He considered that she was developing widespread rheumatoid arthritis and that total hysterectomy might be necessary to stop further developments.

DR. J. B. MCMIKEN said that he regarded sepsis in the uterine cavity as the focal point in the case; the uterus was known to hold infection chronically; pelvic cellulitis and tubular infection were perhaps also present. He had seen two or three instances of a somewhat similar nature in which a succeeding pregnancy had brought considerable relief. He advised curettage of the uterine cavity, treatment of the cervix and encouragement of further pregnancy.

DR. REGINALD MILLS agreed that pelvic infection was the basis and considered that gynæcological surgery was indicated; attempted pregnancy could be used at least as a test of patency of the tubes.

DR. L. J. GURRY suggested that Dr. Browne should present the patient with some *Bacillus coli communis* pus to see if she could recognize its odour and appearance and identify it as similar to the original vaginal discharge. A chocolate cyst might have formed; it could become so dense that a mass formed which could be mistaken for a calculus.

DR. M. ROHAN mentioned a similar patient in whose case pelvic cellulitis has presented over the iliac crest and had subsided when penicillin was used in treatment. She had had two miscarriages and was four months pregnant with extensive pelvic cellulitis still present. She also had complained of symptoms in the vicinity of the right hip joint with some deformity. If Dr. Browne's patient became pregnant the infection was liable to flare up.

Dr. Coates, in concluding the clinical demonstration, congratulated members of the subdivision on the keenness they had displayed and on the thorough nature of the investigations of the patients shown at the meeting. In the case under discussion last, he thought that there was radiological evidence of loss of cartilage and joint involvement. The patient was in a somewhat parlous condition. Perinephric cellulitis was also a possibility. With the use of penicillin they found themselves in a peculiar situation, as it did not clear up local foci of pus in spite of the subsidence of toxic symptoms and febrile states. He suspected a focus in the pelvic wall, and said that that possibility should be explored before the abdomen was opened.

Toxæmias of Pregnancy.

DR. ARTHUR HILL spoke on *hyperemesis gravidarum* and the toxæmias of late pregnancy, with particular reference to treatment. In each instance Dr. Hill began by outlining those features of the current theories of causation which had led to an improvement in the understanding and management of the conditions.

He said that in *hyperemesis gravidarum* theories of causation with a practical application were those of psychosomatic disorder, toxæmia, carbohydrate deficiency and endocrine imbalance. In referring to the pathology in fatal conditions, Dr. Hill said that central necrosis in the liver was not a constant finding, changes in the heart were liable to be atrophic rather than toxic, and in some cases the brain stem had lesions resembling those of Wernicke's encephalopathy.

When hyperemesis proceeded unchecked the progression of events was dehydration, starvation, ketosis, acidosis, liver damage, and finally failure of the liver, adrenals and heart. At the stage of liver failure the body was generally deficient in fluids, glucose, vitamins, salts, minerals and protein, and all those losses must be made good if recovery was to occur. Serious clinical signs were sustained or increasing tachycardia (120 or more per minute), jaundice, persistently low blood pressure, lethargy and cessation of vomiting without a corresponding improvement in the pulse rate or blood pressure, optic neuritis or retinal hæmorrhages, and persistent albuminuria. It was important to determine early the presence of such intrauterine pathological conditions as hydatidiform mole or a dead embryo, and of extragenital causes of vomiting such as pyelitis or intestinal obstruction.

The treatment of *hyperemesis gravidarum* included mild sedation, psychotherapy, isolation from relatives and friends, removal of toxins by aperients and enemata, replacement of fluids and glucose by all routes, occasionally Lugol's solution by mouth or rectum, and intramuscular injections of liver extract, thiamin, pyridoxine, calcium gluconate, and, on rare occasions, "Precortin". In grave conditions protein deficiency should be corrected by intravenous injections of human serum or amino acids. The intravenous restoration of fluids, glucose, calcium and protein should be instituted before the patient had reached the stage at which therapeutic termination of pregnancy was advisable, and the operation should not be delayed until irreversible hepatic, adrenal or myocardial changes had set in. When therapeutic termination had been decided upon it should be performed swiftly, by dilatation and curettage at one sitting or by vaginal or abdominal hysterotomy under gas and oxygen or local analgesia.

Dr. Hill went on to say that the theories of causation of the late toxæmias which had contributed to modern management were those which placed the responsibility chiefly or in part on intestinal toxins (Tweedy), placental toxins (Young), water poisoning (Zangemeister), increased intraabdominal pressure (Paramore), dietetic deficiency, particularly of calcium and vitamins *A*, *B* and *D* (Theobald, Minot and Cutler, Gordon King, Nixon, Browne), Rh and Hr factors, excess of the vasopressor and antidiuretic principles of the posterior pituitary gland (Hofbauer, Hoffmann and Anselmino), and menstrual toxin (Smith and Smith). Of those, the theory of Smith and Smith seemed to correlate most closely the known clinical and biochemical findings, and offered a rational basis for prevention and treatment. Smith and Smith found that toxæmia of late pregnancy was generally preceded for some weeks by a high level of chorionic gonadotropin and a low œstrogenic and progesterone level in the blood and urine, and that the venous serum of toxæmic women contained both the specific menstrual toxin and a protective factor against it. Their practical application of that knowledge consisted in giving large and increasing doses of stilbœstrol from the sixteenth to the thirty-sixth week of pregnancy to potentially or actually toxæmic women, and they were attempting to isolate and concentrate the antitoxic factor by the fractionation of plasma.

Dr. Hill stressed the importance of an early diagnosis of preeclamptic toxæmia. The cardinal signs were hypertension, œdema, oliguria, albuminuria and retinal changes; of those the commonest to appear first was a rise of systolic blood pressure, although œdema was nearly as often first. It was almost certain that albuminuria was never the first sign. Symptoms appeared later and were expressed chiefly through the cerebral, visual, gastro-intestinal and renal systems. Dieckmann had shown that, whereas the mortality rate of cases of toxæmia with signs alone was less than 0·5%, it rose more than fourfold when both signs and symptoms

were present, and more than thirtyfold when convulsions occurred.

The principles of management of preeclamptic toxæmia were good antenatal care, the early detection and treatment of toxæmic signs, and ruthless termination of pregnancy when indicated. In the antenatal period the diet should be rich in proteins, calcium and vitamins *A*, *B* and *D*, and the patient should have regularity of exercise, of rest, of bowel actions, and of attendances at the clinic for weight and blood pressure estimations and urinary analysis.

Dr. Hill discussed in detail the management of the individual signs and symptoms as they arose. For hypertension the most important single measure was rest; other aids included thyreoid extract, additional calcium and vitamins *A* and *B* in the diet, saline aperients, sedatives and ultra-violet light. When the systolic blood pressure exceeded 150 milligrammes of mercury the patient was better in hospital. Renal function tests were of value in detecting occult renal damage and should be repeated at regular intervals if it was decided to continue with the pregnancy in the case of a diagnosis of "essential hypertension". In such a case any exacerbation of the hypertension was serious, while in apparently toxæmic hypertension a systolic blood pressure of 170 millimetres of mercury could be taken as the danger limit. The three great dangers of severe hypertension were fœtal death, accidental hæmorrhage and eclampsia.

The prevention of œdema began with the institution of a proper diet in the early months of pregnancy. A fairly rigid weight control was desirable provided that it did not interfere with adequate nutrition, and the aim should be to restrict the total weight increase to about sixteen pounds, with a maximum of two pounds in any one month. That might prove difficult, but was worth attempting. A diet of a little more than 2000 Calories should contain 120 grammes of protein and be low in salt content. Thyreoid extract, given to an amount just short of intolerance, and "Benzedrine Sulphate" given three times a day to allay hunger could be of value. The development of mild œdema called for a dietary check-up, adequate rest, and saline aperients. With increasing œdema more rest was necessary, sodium should be drastically restricted or entirely eliminated from the diet, and capsules of ammonium chloride, 10 to 20 grains three or four times a day, should be prescribed for periods of five days. When the blood hæmoglobin or protein level was low it should be restored with transfusions of blood, human serum or amino acids. The patient with gross or generalized œdema should be admitted to hospital, and if she did not respond satisfactorily to treatment the pregnancy should be terminated.

In the treatment of oliguria a great advance had been made with the introduction of 20% to 25% glucose in water, given intravenously. It should be employed whenever the daily urinary output fell to one pint, and the total volume given, 600 to 1000 millilitres, should be injected in thirty to forty minutes. That injection could be repeated at intervals of eight to twelve hours if necessary, and in very resistant cases 500 to 800 millilitres of 30% glucose solution should be used.

Albuminuria could be regarded as the "red light", and as soon as it was detected the patient should be admitted to hospital. If, with absolute rest and treatment as already described, the albuminuria did not disappear within five or six days, the pregnancy should be terminated. With albuminuria of any degree a policy of watchful expectancy was rarely, if ever, justified.

The indications for termination of pregnancy were severe hypertension (systolic blood pressure 170 millimetres of mercury or over), gross œdema, albuminuria, retinal changes, and serious symptoms such as persistent headache, epigastric pain and amblyopia. Artificial rupture of the membranes was generally the best method of surgical induction and was increasingly efficient after the thirty-fourth week of pregnancy. The requirements for consistent success were a well-fitting head and a "ripe" cervix. Rectal tubal induction was now rarely employed, its chief dangers being placental separation and intrauterine infection of the baby. Cæsarean section had a definite place, but only with special indications such as rapid increase in the gravity of the toxæmic state despite full general treatment, poor mechanical and hormonic conditions for performing artificial rupture of the membranes, gross vulval œdema, elderly primiparity, disproportion, uterine inertia *et cetera*.

Dr. Hill referred briefly to the treatment of accidental hæmorrhage. He emphasized that in the vast majority of cases the management should be conservative and included sedatives, blood transfusions, the treatment of shock and, when indicated, artificial rupture of the membranes. Judson Smith reported a mortality rate of 21% in 42 cases of treatment by hysterotomy, and Irving a mortality rate of 14% in 69 cases of treatment by Cæsarean section and of 2·9% in 34 cases in which treatment was conservative.

Dr. Hill said that in the treatment of eclampsia magnesium sulphate had been the most important single agent in reducing the mortality rate in recent years. At the Women's Hospital it was given intramuscularly in 50% solution, with ten millilitres as the initial dose, and a further two millilitres for every fit or every four hours while the fits persisted. For very grave conditions the initial dose could be twenty millilitres and the subsequent doses ten millilitres, but at the Women's Hospital the smaller quantities had proved quite satisfactory. Summarized, the Women's Hospital treatment of eclampsia concentrated on the following factors: constant nursing care, morphine sulphate one-quarter of a grain given once only, a high enema, intramuscular injection of magnesium sulphate, at times rectal injection of paraldehyde or intramuscular injection of "Luminal-sodium", 25% glucose solution given intravenously for oliguria, and conservative obstetrics, which usually implied early artificial rupture of the membranes. Chloral hydrate and "Veratrone" were not used, and stomach and bowel washouts had been discarded.

At the Women's Hospital, in the seven years preceding June 30, 1947, there had been 27,230 confinements with 337 cases of eclampsia, an incidence of 1 in 81, or 1·23%. Among those 337 cases the maternal mortality rate was 8% and the fœtal mortality rate 30%. Between January, 1945, and June, 1947, there had been 117 cases of eclampsia treated with intramuscular injections of magnesium sulphate, with a maternal mortality rate of 4%.

Dr. Hill next discussed the value of renal function tests in late pregnancy toxæmia. He thought that those tests were of most value when studied serially; they were a guide to prognosis and management, particularly when the clinical signs were indeterminate or difficult to interpret, as, for example, in cases of mild albuminuria, but without accompanying œdema or a raised blood pressure, of "essential" hypertension, and of chronic pyelitis. At the Women's Hospital the urea concentration excretion test of Kreiger had proved the most delicate and generally useful test. The concentration of urine passed should be above 2%, with a total excretion for three hours of up to six and a half grammes for the first nine months and to within one gramme of that for the last month. The Fowweather test (normal figure 70% to 140%) was chiefly of confirmatory value. The blood urea content should normally be below 25 milligrammes *per centum*; a figure of 30 milligrammes or more indicated renal damage, and of 40 milligrammes or over the need for terminating the pregnancy.

Dr. Hill concluded with the following summary of the chief factors which had made for improvement in the modern management of the late toxæmias: (i) the early and regular check-up and control of blood pressure and weight in addition to routine urinalysis; (ii) a diet rich in proteins, minerals and vitamins; (iii) better control of the biochemistry of the blood, especially its salt, hæmoglobin and protein content; (iv) the early diagnosis and thorough treatment of toxæmic phenomena, and the ruthless termination of the pregnancy when indicated; (v) the intravenous administration of 20% to 25% glucose solution for oliguria; (vi) the intramuscular administration of 50% magnesium sulphate solution for eclampsia; (vii) the wise and free use of oxygen in nursing care and of gas or local analgesia for surgical manœuvres.

DR. M. GURRY, after expressing appreciation of Dr. Hill's informative address on the toxæmias of pregnancy, said that he was glad to note that Dr. Hill was not a devotee of the American school. Dr. Gurry had found often that what he advised his patients was limited by what he knew they could be expected to put into effect. For instance, it was futile early in the piece to say that a woman must go to bed and rest a lot, merely because she was gaining weight more rapidly than usual, or to tell her that she must eat a lot less. At all events the doctor would need a lot of self-confidence and the power to carry conviction with his advice even if in his judgement it was the advice indicated on the evidence. All that could be done in actual practice was to drop a hint or a warning to the close relations and thus influence the patient's way of life obliquely through them. He would like Dr. Hill to give more details about how he produced the desired effect with certainty and what his views were on the procedure of rupture of the membranes and application of a tight binder in induction of labour.

DR. V. L. DAVIES, discussing the criteria set out by Dr. Hill for the early diagnosis of the occurrence of toxæmia, mentioned that he was quite satisfied with a systolic blood pressure in the neighbourhood of 130 millimetres of mercury,

but became very alert if the reading was 135 millimetres or higher. He found it very difficult to secure the attendance of the patients for examination each week for the last eight weeks of pregnancy. He, too, would like Dr. Hill to supply more details about the induction method he practised. He had appreciated the address very much and thanked Dr. Hill for making his points so clearly.

DR. F. R. PHILLIPS said that he would like to join issue with Dr. Hill on the significance of increases in weight. In his opinion the patient before being regarded by him as a candidate for toxæmia would need to show an increase in weight well over and above that used as a warning at the Women's Hospital. He also was not able to keep the blood pressures of his pregnant patients under 130 millimetres of mercury; they often reached 150 millimetres without subsequent trouble. He would like Dr. Hill to give the indications for Cæsarean section in severe toxæmia and suggested a systolic blood pressure above 160 millimetres of mercury and urine described as "half-albumin".

Dr. Hill, in reply, said that in artificial rupture of the membranes he applied a tight binder as a routine part of the procedure. In rupturing the membranes he preferred the tactile method to the visual one. For a *primipara* an anæsthetic was usually administered, but the anæsthetic was not needed when the woman was multiparous. He stripped the membranes by hand and used a single-toothed tenaculum forceps introduced along his finger to make the tear and then opened sufficiently to let the liquor out. He then made a swab preparation in order to be able to study the bacteriology. In the preeclamptic state he did not recommend the Cæsarean operation, but preferred to give the mother a trial of labour after using appropriate chemotherapy and artificial rupture of the membranes when indicated. The baby was liable to die if not delivered within forty-two hours of rupture of the membranes, but by timely chemotherapy and correct management the baby could usually be saved.

Dr. Hill went on to say that the average weight gained in normal pregnancy was twenty-four pounds. Of those who put on weight in excess of that amount more than half became toxæmic and about three-quarters of the patients who were toxæmic put on weight excessively. The advice that was proffered concerning the conduct of the patient during pregnancy should be better than could be expected in actual practice and due allowance should be made for some degree of incomplete compliance. All toxæmic women were more than ordinarily liable to be toxæmic the next time. They were ten times more likely to develop eclampsia if toxæmic or eclamptic in the preceding pregnancy. Finally, Dr. Hill remarked that penicillin or sulphonamide drugs should be used in the management of delayed response after artificial rupture of the membranes.

NEW SOUTH WALES BRANCH NEWS.

THE following is a list of books and journals added to the library of the New South Wales Branch of the British Medical Association during the period July 1, 1947, to January 31, 1948.

Abbie, A. A.: "The Principles of Anatomy", Second Edition, 1946, Sydney; Aguilar, H. D.: "Tumores Broncogenicos", 1946, Buenos Aires; Allen, E. V., and others: "Peripheral Vascular Diseases", 1946, Philadelphia; Aschner, B.: "The Art of Healing", 1947, London.

Baetjer, A. M.: "Women in Industry: Their Health and Efficiency", 1946, Philadelphia; Beaumont, G. E., and Dodds, E. C.: "Recent Advances in Medicine", Twelfth Edition, 1947, London; Bishop, P. M. F.: "Gynæcological Endocrinology", 1946, Edinburgh; Bonney, V.: "Technical Minutiæ of Extended Myomectomy and Ovarian Cystectomy", First Edition, 1946, London; Bowley, A. H.: "The Psychology of the Unwanted Child", 1947, Edinburgh; "British Surgical Practice", edited by Sir E. R. Carling and J. Paterson Ross, Volume I, 1947; Brunner, H.: "Intracranial Complications of Ear, Nose and Throat Infections", 1946, Chicago; Brunschwig, A.: "Radical Surgery in Advanced Abdominal Cancer", 1947, Illinois; Buchanan, A. M.: "Manual of Anatomy", edited by F. Wood Jones, Seventh Edition, 1946, London; Burnet, F. M.: "Virus as Organism", 1946, Cambridge; Burn, J. L.: "Recent Advances in Public Health", 1947, London.

Cameron, A. T.: "Recent Advances in Endocrinology", Sixth Edition, 1947, London; Cameron, H. C.: "Nervous Child", Fifth Edition, 1946, London; Chalmers, C. H.: "Bacteria in Relation to the Milk Supply", Third Edition, 1945, London; Clark, W. E. Le Gros: "Practical Anatomy", 1946, London; Collens, W. S., and Boas, L. C.: "Modern Treatment of Diabetes Mellitus", 1946, Illinois; Commonwealth of Australia: "Report of the National Health and Medical Research Council", 23rd Session, June, 1947, Canberra; Cooke, R. A.: "Allergy in Theory and Practice", 1947, Philadelphia; Craig, W. S.: "Child and Adolescent Life in Health and Disease", 1946, Edinburgh; Conybeare, Sir J.: "Textbook of Medicine", Eighth Edition, 1946 London; Curtis, A. H.: "Textbook of Gynecology", Fifth Edition, 1946, Philadelphia.

Davison, W. C.: "The Compleat Pediatrician", Fifth Edition, 1946, Durham, N.C., and Fourth Edition, 1943; Day, Sister M. A. C.: "Basic Science in Nursing Arts", Second Edition, 1947, St. Louis; Derbes, Vincent J., and Engelhardt, Hugo T.: "Treatment of Bronchial Asthma", 1946, Philadelphia; Dobson, J.: "Anatomical Eponyms", 1946, London.

East, W. Norwood: "Introduction to Forensic Psychiatry in the Criminal Courts", 1927, London; Edinburgh Post-Graduate Lectures in Medicine, Volume III, 1942-1943, 1946, Edinburgh; Elman, R.: "Parenteral Alimentation in Surgery", 1947, New York; Engle, E. T.: "Proceedings of Conference on Diagnosis in Sterility", Springfield, 1946, edited by E. T. Engle; English, Sir Crisp: "Patients and Appendicitis", 1946, London; Ewart, E. D.: "A Guide to Anatomy", Sixth Edition, 1947, London.

Fairbrother, R. W.: "A Textbook of Medical Bacteriology", Fifth Edition, 1946, London; Fanu, W. R. Le: "List of Medical Libraries and Information Bureaux in the British Isles", 1946, London; Fearon, W. R.: "Introduction to Biochemistry", Third Edition, 1946, London; Fletcher, E.: "Medical Disorders of the Locomotor System", 1947, Edinburgh; Garrod, A. C., and others: "Diseases of Children", Third Edition, 1947, 2 Volumes, London; Geikie-Cobb, I.: "The Glands of Destiny", Third Edition, 1947, London; Ghosh, B. N.: "Pharmacology, Materia Medica and Therapeutics", Seventeenth Edition, 1946, Calcutta; Gibberd, G. F.: "A Short Textbook of Midwifery", Fourth Edition, 1947, London; Goldring, W., and others: "Experimental Hypertension", Volume III, 1946, New York; Gray, H.: "Anatomy, Descriptive and Applied", Twenty-Eighth Edition, 1944, London; Graybiel, Ashton and White, P. D.: "Electrocardiography in Practice", Second Edition, 1946, Philadelphia; Green, B. M.: "Modern Audiometric Technique", 1948, Melbourne.

Hadfield, G., and Garrod, L. P.: "Recent Advances in Pathology", Fifth Edition, 1947, London; Hamilton, A., and Johnstone, R. T.: "Industrial Toxicology", 1945, New York; Hamilton-Paterson, J. L.: "Penicillin in General Practice", 1946, London; Harries, E. H. R., and Mitman, M.: "Clinical Practice in Infectious Diseases", Third Edition, 1947, Edinburgh; Harry-Price, Hoel: "Short Handbook of Practical Anæsthetics", 1946, Bristol; Hawk, P. B., Oser, B. L., and Summerson, W. H.: "Practical Physiological Chemistry", Twelfth Edition, 1947, London; Hill, C.: "Your Body: How it Works and How to Keep it Working Well", 1944, London; Houliston, M.: "The Practice of Mental Nursing", 1947, Edinburgh; Hutchinson, H.: "Jonathan Hutchinson: Life and Letters", 1946, London.

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Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Numbers 46 and 49, of March 18 and 24, 1948.

AUSTRALIAN MILITARY FORCES.

Interim Army.

Australian Army Medical Corps.

To be Temporary Brigadier, 14th October, 1947.—WX10 Lieutenant-Colonel (Temporary Colonel) J. H. Stubbe, E.D.

Short Service Commission: To be Captain.—NX208064 Captain D. C. Cook, Australian Army Medical Corps (Medical), 27th January, 1948.

SX700021 Captain P. G. Jay is transferred to the Reserve of Officers (Australian Army Medical Corps) (4th Military District), 20th January, 1948.

Reserve of Officers.

Australian Army Medical Corps.

The following officers are transferred to the Reserve of Officers of the Military Districts shown on the dates indicated. Officers holding temporary rank relinquish such temporary rank with effect from the date of transfer to the Reserve of Officers:

NX204413 Captain (Temporary Major) P. G. Middleton (2nd Military District), 15th January, 1948 (in lieu of the notification respecting this officer which appeared in Executive Minute No. 11 of 1948, promulgated in *Commonwealth Gazette* No. 22 of 1948).

SX33981 Captain R. A. Burston (4th Military District), 17th January, 1948, and SX33991 Captain (Temporary Major) M. W. Elliott (4th Military District), 20th January, 1948.

130*th General Hospital.*—QX64243 Captain J. A. Nye (1st Military District), 10th January, 1948.

Active Citizen Military Forces.

Australian Army Medical Corps.

V600039 Major F. R. Matyear is appointed from the Reserve of Officers (Australian Army Medical Corps) (3rd Military District) (part-time duty), 4th December, 1947.

Reserve Citizen Military Forces.

Australian Army Medical Corps.

3rd Military District.—Major C. T. Stephen is placed upon the Retired List (3rd Military District) with permission to retain his rank and wear the prescribed uniform, 29th January, 1948.

The following officers are retired, 29th January, 1948: Honorary Captains E. A. North, C. C. Reid and A. R. Tate.

6th Military District.—Major F. W. Fay, M.C., is placed upon the Retired List (6th Military District) with permission to retain his rank and wear the prescribed uniform, 19th January, 1948.

1st Military District.—The notification respecting Major C. R. Morton, which appeared in Executive Minute No. 181 of 1947, promulgated in *Commonwealth Gazette* No. 241 of 1947, is withdrawn.

3rd Military District.—Lieutenant-Colonel Sir H. G. Smith, V.D., is placed upon the Retired List (3rd Military District) with the honorary rank of Colonel and with permission to wear the prescribed uniform, 13th February, 1948.

4th Military District: To be Honorary Captain, 3rd February, 1948.—Charles Graham Wilson.

ROYAL AUSTRALIAN AIR FORCE.

Citizen Air Force: Medical Branch.

The part-time appointment of Temporary Wing Commander D. G. Carruthers (263952) is terminated, 2nd February, 1948, on cessation of part-time duties.

Reserve: Medical Branch.

Ex-Wing Commander Douglas Gordon Carruthers (263952) is appointed to a commission, 3rd February, 1948, with the temporary rank of Wing Commander.

Special Correspondence.

CANADA LETTER.

FROM OUR SPECIAL CORRESPONDENT.

CANADIAN medical circles have been shocked by the sudden death of two of its eminent surgeons. Dr. Roscoe Graham, the gastric surgeon of Toronto, died at Collingwood, Ontario, while on a skiing holiday. Dr. Fraser Gurd, Professor of Surgery at McGill University, died in his railway compartment while on his way to Chicago to address a surgical meeting. Dr. Graham had been associated with the Toronto General Hospital for many years. Dr. Gurd brought the teaching methods of the Montreal General Hospital up to a high standard and carried on much original research on burns and their treatment.

The Dominion Bureau of Statistics has just reported that the net loss in doctors to the United States annually from Canada is 206 for the past year. About 10% of the graduates of Canadian schools migrate to the United States of America, either for post-graduate training and eventual teaching posts, or for opportunities in practice. The cost of living in the United States of America has, however, risen to such astronomical heights that this practice may soon decrease considerably.

A final report by the Metropolitan Life Insurance Company on causes of death among physicians has recently come before the Canadian profession. The report does much to fill in the gaps which were always a source of argument in past discussions, such as those by Willius in the United States of America, and by some of his British counterparts. Almost three-quarters of medical practitioners die from the standard five leading causes, as follows: diseases of the heart and coronary arteries, 40·7%; cerebro-vascular accidents and other intracranial lesions, 10·8%; cancer, 10%; nephritis, 6%; pneumonia and influenza, 5·5%, *et cetera*.

As compared with other white males of the same age, medical practitioners experience 120% of the cerebral hæmorrhage, 116% of the arteriosclerosis and 118% of the coronary disease and heart disease reported. For coronary disease alone, doctors suffer 181% of the normal incidence. Only part of this disturbing propensity to coronary occlusion can be accounted for on the basis of better diagnosis in the case of medical practitioners themselves. It is a commonplace that doctors are the last in the community to be diagnosed as having any ailment until it is too late. In a similar manner, leuchæmia in doctors equals 175% of that in the white male population of the same age group.

It is in the infectious diseases and those complaints amenable to surgery that doctors fare better than the general population. Syphilis is only one-third as common, tuberculosis less than half as common, appendicitis about 75% and cancer 80% as common as a cause of death as in the overall adult male population. In automobile accidents, unfortunately, the doctor competes with the average in 90% of cases.

It would appear, therefore, that coronary disease is disproportionately high in the lives of doctors, and certainly as a cause of death, in the United States. It remains to be confirmed in other countries, especially those in which there is a more evident disposition to relax after luncheon and to take a little time out for tea. The relevance of some such preventive can be readily adduced from the following figures released by the United States Public Health Service: the life expectancy of a doctor at age 25 is 42 years, for 39·4 years of which he will be gainfully employed, although in "full service" only 27·7 years. At age 30, his life expectancy is 37·6 years, the remaining years of gainful employment are 35·1, and the term of "full service" being 26 years.

Correspondence.

LA DOULEUR.

Sir: Your reviewer (March 20, 1948, page 374) has taken to task M. Paul Chauchard for ignoring "the fact that no one has ever succeeded in eliciting a painful feeling by stimulating the cortex in a conscious human patient".

This "fact" is refuted by Foerster[1] and by Penfield and Boldrey,[2] who recorded in 163 patients more than 800 sensory responses to stimulation of the cortex by electricity. Twelve of these responses were painful. "This", said the authors, "would seem to be contradictory to the statement made elsewhere . . . that the brain is insensitive. . . ." In the earlier contribution, Penfield[3] had recorded intracranial pain responses from 34 patients trephined under local analgesia. In three of these (cases 7, 19 and 22) he observed that the brain was painful to mechanical stimuli after it had been separated from the dura. But he made no comment on the observation. Of Penfield and Boldrey's 800 responses, only two were described as hot and thirteen as cold, while there never was a clear sensation of touch or contact. In nearly 90% the feeling was described as tingling, electricity, numbness or a sense of movement. The responses, said Penfield and Boldrey, are crude and give only a caricature of true physiological function. With stronger stimuli Horrax[4] recently elicited pain from the post-central cortex in three out of four patients.

Some clinical evidence, too, suggests that pain may be produced in the cortex. (i) Pain may occur as an epileptic aura.[5][6] (ii) "Paroxysmal spontaneous pain in the periphery of a limb . . . sometimes occurs . . . in gross disease of the cortical sensory areas. . . ."[6] Michelsen,[6] when reviewing the subject recently, gave details of five such cases. (iii) Intractable pain (for example, phantom limb) can be abolished by removal of the appropriate area in the sensory cortex, though it usually recurs within a few weeks.[6][7]

Earl Walker,[8] who emphasizes the importance of the cortex in the appreciation of pain, wrote:

> The fact that pain is relatively little influenced by small cortical lesions is the result of the numerous pathways which are open to it to reach the cerebral cortex. The function of the thalamus is thus not so much the appreciation of pain as its integration with other sensory modalities.

Thus Chauchard is not alone in rejecting Head's view of the function of the thalamus. F. M. R. Walshe[9] has written:

> It is clear that Head's theory of the morphological constitution of the afferent nervous system is invalid, and that Jackson's doctrine of release of function has proved singularly disappointing as a generalization of the observed facts of sensory loss from lesions of the nervous system.

Yours, etc.,

Michael Kelly.

417, St. Kilda Road,
Melbourne,
March 22, 1948.

References.

(1) O. Foerster: *"Sensible Corticale Felder"*, *"Handbuch der Neurologie"*, Volume VI, 1936, page 358.

(2) W. Penfield and E. Boldrey: "Somatic Motor and Sensory Representation in the Cerebral Cortex of Man as Studied by Electrical Stimulation", *Brain*, Volume LX, 1937, page 389.

(3) W. Penfield: "A Contribution to the Mechanism of Intracranial Pain", *Proceedings of the Association for Research in Nervous and Mental Disease*, Volume XV, 1934, page 399.

(4) G. Horrax: "Experiences with Cortical Excisions for Relief of Intractable Pain in the Extremities", *Surgery*, Volume XX, 1946, page 593.

(5) L. Mann: *"Ein ungewöhnlicher Fall von traumatische Spätepilepsie mit sensibler neuralgiformer Aura, encephalographisch nachgewiesen"*, *Klinische Wochenschrift*, Volume IX, 1930, page 218; W. Penfield and L. Gage: "Cerebral Localization of Epileptic Manifestations", *Archives of Neurology and Psychiatry*, Volume XXX, 1933, page 709; J. J. Michelsen: "Subjective Disturbances of the Sense of Pain from Lesions of the Cerebral Cortex", *Proceedings of the Association for Research in Nervous and Mental Disease*, Volume XXIII, 1943, page 86.

(6) Purves Stewart: "The Diagnosis of Nervous Diseases", Third Edition, 1911, page 188.

(7) C. G. de G. Mahoney: "The Treatment of Painful Phantom Limb by Removal of Post-Central Cortex", *Journal of Neurosurgery*, Volume I, 1944, page 156; H. Trumble: Report to Alfred Hospital Clinical Society, Melbourne, 1945.

(8) A. E. Walker: "Central Representation of Pain", *Proceedings of the Association for Research in Nervous and Mental Disease*, Volume XXIII, 1935, page 63.

(9) F. M. R. Walshe: "The Anatomy and Physiology of Cutaneous Sensibility: A Critical Review", *Brain*, Volume LXV, 1942, page 48.

THE DIAGNOSIS, PREVENTION AND TREATMENT OF PUERPERAL INFECTION.

Sir: In the article "The Diagnosis, Prevention and Treatment of Puerperal Infection", published in the journal of February 21, 1948, we have inadvertently omitted two small passages which are important to the clinical balance of the article. We would be grateful if you could publish this letter so that the omitted passages can be inserted by anyone who uses the article for reference.

The first passage is omitted from page 230, under the section "Infection Spreading Beyond the Birth Canal but Localized to the Pelvis", and should follow directly on that section's second last paragraph which ends with the words "pelvic cellulitis". The passage omitted reads:

> Figure V is from a case of pelvic cellulitis treated before the introduction of modern chemotherapy. The comparatively slow pulse rate in association with a swinging temperature is characteristic.

The second passage is omitted from page 233 under the heading "Conduct of Labour", and should follow directly on the opening sentence which ends with the words "operative interference". The passage omitted reads:

> Of particular importance is careful management of the third stage, with reduction to a minimum of blood

loss, and its rapid replacement when of undue amount. Were it routine practice to restore the patient's blood volume and hæmoglobin content to normal levels at the end of labour the incidence and severity of the common anaerobic infections would be significantly reduced.

Yours, etc.,

A. M. HILL.
H. M. BUTLER.

317, Glenferrie Road,
Malvern, S.E.4,
Victoria.
March 26, 1948.

DOSES OF PROPRIETARY PREPARATIONS.

SIR: I notice that in certain proprietary cough syrup it is stated, "contains ethylmorphine hydrochloride 0·02 per cent.". One is too busy to work out the actual dose a patient is taking. It is a much better practice to let us know that "one fluid drachm or ounce contains gr. . . .". I hope that this catches the eyes of manufacturers.

Yours, etc.,

J. S. BARR-DAVID.

120, Boundary Street,
West End, Brisbane, S.1.
March 21, 1948.

THE TREATMENT OF PSYCHOSES AND PSYCHO-NEUROSES BY ELECTROPLEXY (ELECTRIC SHOCK THERAPY) IN A GENERAL HOSPITAL.

SIR: I am grateful to Professor Bostock and Dr. Phillips for their reply in your issue of March 20, but the innocent ingenuousness of their statement that "Pentothal Sodium" cannot produce a psychosis indicates the reason for such an assertion of the obvious, namely, it is a red herring.

They evade the point I made that, in their excellent article in which they make the highly responsible claim that electric shock convulsions can be used for diagnostic purposes, they give no evidence to support this view.

If now their declared evidence is that "Pentothal", the anæsthetic, is analogous to electroplexy, the convulsant, because the patients are in a state of cathartic confusion after their use, then I am free to state my opinion, which is that the sooner the authors stop using electro-convulsive shocks for diagnostic purposes on patients who before their use are suffering only from psychoneurosis, then the better it will be for everybody.

Yours, etc.,

JOHN A. MCCLUSKIE,
Psychiatrist Specialist.

Department of Repatriation,
Perth,
March 27, 1948.

THE CRAWFORD MOLLISON PRIZE.

SIR: Almost twelve months ago the staff of the Women's Hospital, Melbourne, resolved to recognize the great services of Dr. Crawford Henry Mollison by the establishment of a triennial prize. This decision has the earnest support of the Council of the Victorian Branch of the British Medical Association.

The services of Dr. Mollison to this community have been unique. Besides the many positions he has held with distinction, Dr. Mollison was honorary treasurer of the Victorian Branch of the British Medical Association for more than fifty years, a period without precedent in the history of the Association.

Dr. Mollison now lives in retirement in the hills near Melbourne, and the attention of medical graduates throughout Australia who have come under his influence is again invited to this opportunity of paying tribute in a permanent manner to the great name and the great services of Crawford Henry Mollison.

Yours, etc.,

F. KINGSLEY NORRIS,
President.

Victorian Branch of the British Medical Association,
Medical Society Hall,
426, Albert Street,
Melbourne.
March 24, 1948.

Medical Prizes.

THE CRAWFORD MOLLISON PRIZE.

To commemorate the great services rendered to medicine in Australia by Dr. Crawford Henry Mollison as a practising pathologist for over fifty years, it is proposed to establish a Crawford Mollison Prize under the following conditions:

1. The establishment of a capital fund of not less than £1000 to be vested in trustees.

2. The prize to be the sum of one hundred guineas to be awarded triennially for the most notable contribution to pathology during that triennial period.

3. The recipient(s) of the prize to be a graduate(s) of the University of Melbourne for work carried out anywhere in the British Empire or graduate(s) of another medical school for work done in the State of Victoria.

4. The prize to be awarded by a committee composed of the trustees of the fund, the dean of the Faculty of Medicine in the University of Melbourne, the Professor of Pathology in the University of Melbourne, the Professor of Experimental Medicine in the University of Melbourne, the Professor of Obstetrics in the University of Melbourne, and the chairman of the honorary medical staff of the Women's Hospital, Melbourne.

5. The trustees to have the right to require the recipient(s) of the prize to present to the medical profession the work for which the award was made, either by publication or by lecture.

To provide the necessary funds a capital sum of not less than £1000 will be required, and a subscription list, to which all Dr. Mollison's former students, colleagues and friends are invited to subscribe, is now open.

The list is headed by a contribution of £250 from the honorary medical staff of the Women's Hospital, Melbourne, and to date £49 17s. 6d. has been subscribed in addition. Contributions should be forwarded to the Medical Secretary, British Medical Association (Victorian Branch), 426, Albert Street, East Melbourne, C.2, Victoria, cheques being made payable to the "Mollison Prize Fund".

Research.

THE GEORGE ADLINGTON SYME SCHOLARSHIP, 1949.

THE Council of the Royal Australasian College of Surgeons invites applications for the George Adlington Syme Research Scholarship for 1949. The scholarship is valued at £50.

Applicants are requested to give full details of the research work which they desire to undertake. It is preferable that the research should be clinical in nature. The successful applicant must undertake to publish, in *The Australian and New Zealand Journal of Surgery*, a paper recording the results of his or her work, or to present the result at a lecture to be arranged, should the Council so desire. Any further information required may be obtained from the Secretary of the College, Spring Street, Melbourne, with whom applications must be lodged on or before July 1, 1949.

Obituary.

FREDERIC JOHN CHAPPLE.

DR. FREDERIC JOHN CHAPPLE, whose death occurred on January 22, 1948, was born in England on February 2, 1871, but came to Australia at an early age when his father was appointed Headmaster of Prince Alfred College, Adelaide. Dr. Chapple was educated at that school, and he gained the Robb Scholarship in 1886, the Colton Scholarship in 1887, the Old Scholar's Scholarship in 1888, and in 1889 he gained a University Scholarship and proceeded to the University of Adelaide, where he obtained his B.Sc. degree in 1891. He then entered the medical course and was one of the students who was compelled to complete his course at the University of Melbourne owing to the disputes and resignations among the staff at the Adelaide Hospital.

After gaining his degree in 1897 he proceeded to Queensland, where he was superintendent of the Rockhampton Hospital until 1905, when he returned to Adelaide and was appointed superintendent of the Adelaide Hospital. After a few years in that position he entered general practice at Nairne and Clarendon. In 1914 he was engaged in war service at Keswick Hospital (military), having been refused permission to proceed overseas on account of age. At the conclusion of the 1914-1918 war he entered into partnership at Parkside with Dr. Sweetapple, and then continued in practice alone until his final illness. He had an extensive practice in that suburb until some three years ago when he was involved in a serious motor accident from the effects of which he never completely recovered. He had a wide circle of friends, and during his stay at Clarendon he entered into the community life of that district, but subsequent to the war he was too engrossed in practice to continue these outside activities.

Following on his accident three years ago he was compelled to relinquish practice, and for the last two years had been bedridden in hospital.

PAUL ERNEST VOSS.

PAUL ERNEST VOSS, whose death has been announced in this journal, was the elder son of Dr. F. H. V. Voss and helped his father to make theirs for over sixty years the best known name in the medical life of central Queensland.

His school days were spent at the Rockhampton Grammar School and the Church of England North Shore Grammar School. In 1911 he went up to Saint Paul's College at the University of Sydney; he graduated with honours in medicine and was a resident medical officer at Royal Prince Alfred Hospital until joining the Australian Imperial Force. Voss was an excellent oar, rowing for several years with the university crew, and was chosen to go to Stockholm with the Olympic eight. In France he was wounded on several occasions and was awarded the Military Cross.

On returning to Australia in 1919 he married Dr. Harriette M. Exton and joined his father and Dr. Davidson in practice at Rockhampton, where he remained until his death.

Surgery, particularly gynæcology, was his main interest, and in 1929 he was elected a Fellow of the Royal Australasian College of Surgeons.

Nominations and Elections.

THE undermentioned has applied for election as a member of the New South Wales Branch of the British Medical Association:

Cary, Wilfred Hezlet, M.B., B.S., 1946 (Univ. Sydney), Cumberland, 452, Edgecliff Road, Edgecliff.

Books Received.

"Progress in Clinical Medicine", by various authors, edited by Raymond Daley, M.A., M.D. (Camb.), M.R.C.P., and Henry G. Miller, M.D. (Durham), M.R.C.P., D.P.M.; 1948. London: J. and A. Churchill, Limited. 9¼" x 6", pp. 368, with illustrations. Price: 21s.

"Materia Medica: Pharmacy, Pharmacology and Therapeutics", by William Hale-White, K.B.E., M.D. (London), M.D. (Dublin), LL.D. (Edinburgh), revised by A. H. Douthwaite, M.D., F.R.C.P.; Twenty-Seventh Edition; 1947. London: J. and A. Churchill, Limited. 7¼" x 5", pp. 560. Price: 15s.

"Chronic Ill-Health Relieved by Drainage of the Para-Nasal Sinuses", by Rosa Ford, M.B. (London), D.O. (Oxon.); 1948. London: Henry Kimpton. 7¼" x 4¾", pp. 116. Price: 6s.

"Psychiatric Examination of the School Child", by Muriel Barton Hall, M.D.; 1947. London: Edward Arnold and Company. 8½" x 5½", pp. 376. Price: 15s.

"Infant Feeding", by Vernon L. Collins, M.D. (Melbourne), M.R.C.P. (London), D.C.H. (London); Fifth Edition; 1948. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 8½" x 5½", pp. 98. Price: 5s. 6d.

"A Text-Book of Mental Deficiency (Amentia)", by A. F. Tredgold, M.D., F.R.C.P., F.R.S. (Edinburgh); Seventh Edition; 1947. London: Baillière, Tindall and Cox. 8½" x 5½", pp. 550, with many illustrations. Price: 30s.

"Outline of Law in Australia", by John Baalman; 1947. Sydney, Melbourne and Brisbane: The Law Book Company of Australasia Proprietary, Limited. 7" x 4¾", pp. 368.

Diary for the Month.

APRIL 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
APRIL 15.—Victorian Branch, B.M.A.: Organization Subcommittee.
APRIL 19.—Victorian Branch, B.M.A.: Finance, House and Library Subcommittee.
APRIL 20.—New South Wales Branch, B.M.A.: Medical Politics Meeting.
APRIL 21.—Western Australian Branch, B.M.A.: General Meeting.
APRIL 22.—New South Wales Branch, B.M.A.: Clinical Meeting.
APRIL 22.—Victorian Branch, B.M.A.: Executive Meeting.
APRIL 23.—Queensland Branch, B.M.A.: Council Meeting.
APRIL 27.—New South Wales Branch, B.M.A.: Ethics Committee.
APRIL 28.—Victorian Branch, B.M.A.: Council Meeting.
APRIL 29.—New South Wales Branch, B.M.A.: Branch Meeting.
APRIL 29.—South Australian Branch, B.M.A.: Branch Meeting.
MAY 4.—New South Wales Branch, B.M.A.: Organization and Science Committee.
MAY 5.—Western Australian Branch, B.M.A.: Council Meeting.
MAY 5.—Victorian Branch, B.M.A.: Branch Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute; Brisbane City Council (Medical Officer of Health). Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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